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RUPTURE OF THE INTERVENTRICULAR SEPTUM*

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AMONG the complications that may plague the patient with myocardial infarction, there are few more dramatic or serious than rupture through an infarct involving the interventricular septum. To be sure, it is a rare phenomenon, but when it does occur the subsequent rapid course to termination frequently makes clinical detection difficult if not impossible. However, when time permits and one is aware of the syndrome, the ante-mortem diagnosis can readily be made.

In 1845 the syndrome was first reported by Latham.[1] There were occasional reports in the literature up to 1923, when Brunn[2] described 2 cases and recorded the first ante-mortem diagnosis. Only 17 case reports had been published until 1934, when Sager,[3] in an excellent review of the literature, reported an additional case. Until 1943, a total of 36 cases had been noted. Fowler and Failey[4] included in their review up to May, 1948, a total of 60 cases of acquired interventricular septal defect complicating myocardial infarction, of which 17 had been diagnosed ante mortem. Two additional cases in which the diagnosis was made before death have been reported.[5, 6]

In the following 4 cases of acquired interventricular septal defect occurring during the course of myocardial infarction the ante-mortem diagnosis was confirmed at autopsy in 3.

CASE REPORTS

CASE 1. W. S. (Q. G. H. 3997), a 67-year-old man, was admitted to the hospital on April 21, 1946. Six years previously he had suffered a myocardial infarction. Three hours before admission he was suddenly seized with severe persistent retrosternal pain, radiating to the left shoulder.

Physical examination revealed an acutely ill man who was cyanotic, apathetic and dyspneic. The blood pressure was 140/90. Fine moist rales were audible at the lung base. The heart sounds were of moderately good quality, with regular sinus rhythm and no murmurs; the aortic second sound was greater than the pulmonic. The remainder of the examination was negative. The urine gave a ++ test for albumin. The blood urea nitrogen was 29 mg. per 100 cc. The white-cell count was 14,000; the sedimentation rate was 24 mm. per hour corrected (Wintrobe method). The blood Wassermann reaction was negative.

A diagnosis of hypertensive and arteriosclerotic heart disease, coronary sclerosis and occlusion, with myocardial infarction, was made.

On the following day, an electrocardiogram revealed changes indicative of recent anterior-wall infarction (Fig. 1).

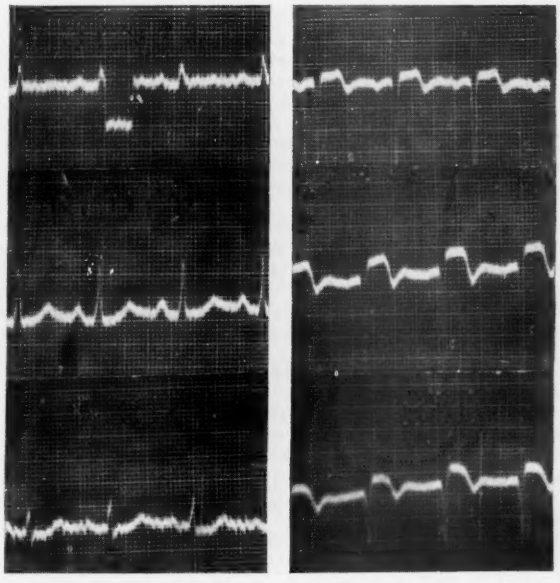

FIGURE 1. *Tracings in Case 1, Showing Regular Sinus Rhythm, a PR Interval 0.20 Second and QRS Complex of 0.08 Second. The T waves are isoelectric in Lead 1 and upright in Lead 2, being greater in Lead 3 than in Lead 1. The chest leads show elevated RST segments, absent R waves and inverted T waves.*

On the 5th hospital day his condition was reported as improved. The heart tones were good, and there were no murmurs.

On the 6th day he complained of severe chest pain, dyspnea, nausea and vomiting. The blood pressure was unobtainable, and the pulse was rapid and thready; over the precordium a harsh, blowing, moderately long, moderately loud systolic murmur was heard. The murmur was loudest at the left lower sternal margin and faded toward the axilla. No thrill could be palpated; the aortic second sound was now equal to the pulmonic. A diagnosis of rupture of the

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septum was made. The murmur, without thrill, remained audible until the patient suddenly died approximately 16 hours after the estimated time of the perforation of the interventricular septum and on the 6th day after the coronary occlusion. An electrocardiogram taken prior to death was essentially unchanged.

At post-mortem examination* the heart was enlarged, weighing 550 gm. The interventricular septum and the left ventricle anterior to it were softened and yellow brown. There was a fresh thrombus in the left anterior descending coronary artery distal to its bifurcation. The infarction of

FIGURE 2. *Gross Appearance of the Heart in Case 1, Showing Left Side of the Heart, with the Perforation Visible in the Anterior Superior Aspect of the Interventricular Septum.*

the anterior two thirds of the septum extended to within 1 cm. of the bundle of His, with a rupture of the septum at its upper portion between right and left ventricles (Fig. 2).

The pathological diagnoses were coronary arteriosclerosis, thrombosis of the left anterior descending coronary artery, with infarction of the interventricular septum and anterior wall, and rupture of the interventricular septum.

CASE 2. W. M. (Q. G. H. 8420), a 44-year-old man, was admitted to the hospital on August 10, 1946. Three days previously there had been an abrupt onset of epigastric pain, going from the epigastrium into the left upper quadrant. The pain lasted approximately 2 hours and was associated with nausea, vomiting and diarrhea. By the day of admission the temperature had risen to 103°F. Hypertension (blood pressure of 200/100) had been discovered 10 months prior to the present episode.

Physical examination revealed a temperature of 103°F., pulse of 160 and respirations of 32. The blood pressure was unobtainable. The lungs were clear. There was a regular sinus tachycardia (rate of 160), with a harsh, blowing precordial systolic murmur associated with a systolic thrill, less intense at the aortic region. Both the aortic and the pulmonic second sounds were inaudible.

Examination of the blood showed a red-cell count of 4,800,000, with a hemoglobin of 14 gm., and a white-cell count of 14,000, with 85 per cent neutrophils and 15 per cent lymphocytes. The corrected sedimentation rate was 5 mm. per hour (Wintrobe method).

The diagnosis was hypertensive and arteriosclerotic heart disease with coronary-arteriosclerosis, occlusion and myocardial infarction. Because of the harsh systolic precordial murmur and thrill, a diagnosis of rupture of the interventricular septum was also made.

The patient was treated with oxygen, morphine, 8 cc. of Cedilanid and adrenocortical extract and 250 cc. of plasma. His condition remained poor. There was a regular sinus tachycardia of 124 per minute, and the harsh systolic murmur noted over the precordium was most pronounced over the right xiphoid process. The patient died on the 4th day.

At post-mortem examination† the pericardial cavity contained 100 cc. of sanguineous fluid. The heart was enlarged, weighing 500 gm. There was an area of infarction of the posterosuperior wall of the left ventricle and the upper and lower posterior portions of the interventricular septum. In this lower area the septum had ruptured with a resulting 2-cm. communication near the apex posteriorly. The perforation was fringed by ragged, soft, necrotic muscle and thrombus. The coronary arteries showed marked atherosclerosis. The left circumflex coronary artery contained an organizing thrombus 2 cm. from its origin (Fig. 3).

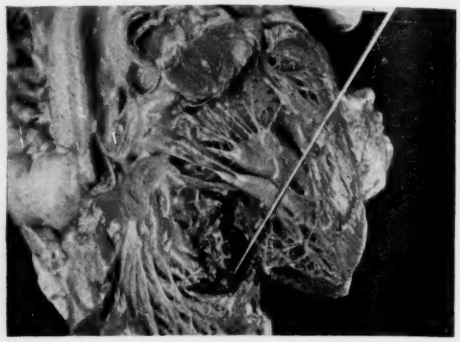

FIGURE 3. *Appearance of the Heart in Case 2, Showing Left Ventricle with Perforation in the Posterior Portion of the Interventricular Septum.*

The pathological diagnoses were coronary arteriosclerosis, thrombosis of the left circumflex coronary artery, with infarction of the interventricular septum and posterior wall, and rupture of the interventricular septum.

CASE 3. F. K., a 69-year-old man, was admitted to the hospital on December 24, 1947. Three weeks prior to admission the patient had had repeated attacks of substernal pain on exertion. On December 23 severe precordial pain appeared, persisting up to the time of admission.

Physical examination revealed an elderly man with only moderate dyspnea after administration of 10 mg. (1/6 gr.) of morphine sulfate. The blood pressure was 40/0, the pulse 68, and the respirations 28. The lungs were clear. The heart rhythm was irregular; the sounds were of good quality and a systolic murmur, otherwise undescribed, was audible at the apex. The extremities showed cyanosis of the fingers and toes.

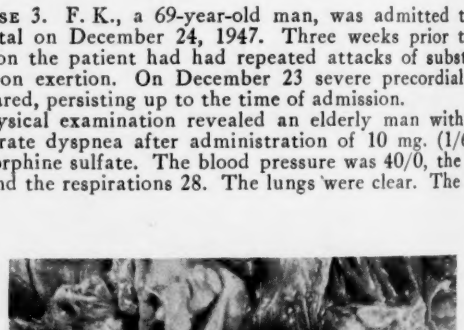

FIGURE 4. *Appearance of the Heart in Case 3, Showing Perforation of the Posterior Portion of the Septum.*

A diagnosis of arteriosclerotic heart disease, with coronary arteriosclerosis, occlusion with myocardial infarction and cardiogenic shock, was made.

The patient was given fluids intravenously and plasma, oxygen and morphine. His condition remained poor, and he was found dead on the 2nd day of the acute illness.

*Performed by Dr. W. Eichacker (No. A-46-204).

†Performed by Dr. F. Weinberg (No. A-46-376).

At post-mortem examination* the heart was larger than usual. The posterior part of the septum was mottled and hemorrhagic, with definite yellow fatty areas. There was a rent, 3 cm. in length, in the interventricular septum, involving the posterior part and creating a communication between the ventricles. The left anterior descending coronary artery was occluded 3.5 cm. from the left coronary ostium (Fig. 4).

The pathological diagnoses were marked coronary arteriosclerosis, thrombosis of the left anterior descending coronary artery, with infarction of the posterior wall and the interventricular septum, and rupture of the infarcted interventricular septum.

Case 4. W. W. (Q. G. H. 52350), a 68-year-old man, was admitted to the hospital on January 8, 1948. The patient had noted mild exertional dyspnea, orthopnea and intermittent ankle edema for the past year. Three weeks prior to admission he was suddenly seized with a severe retrosternal pain associated with dyspnea. After several hours the pain diminished, and shortly thereafter blood-tinged sputum was expectorated. For over 30 years a mild productive cough had been present, with rare blood streaking of the sputum.

Physical examination revealed an acutely and chronically ill cyanotic man. There were numerous basal, fine, moist rales, and over the right upper lobe the breath sounds appeared bronchial, with crackling, moist rales. The rhythm was regular, the rate rapid, and the heart sounds indistinct. A loud, moderately long, blowing, systolic murmur was heard over the whole precordium, being loudest over the apex and lower left parasternal area. The pulmonic second sound was greater than the aortic. There was a slight sacral and pretibial edema.

The temperature was 100°F. by mouth, the pulse 100, and the respirations 36. The blood pressure was 112/82.

Examination of the blood showed a white-cell count of 20,500, with 80 per cent neutrophils. The sedimentation rate was 20 mm. per hour. An electrocardiogram demonstrated regular sinus rhythm, with vertical axis and evidence of posterior-wall infarction in the limb leads and anteroseptal infarction in the chest leads.

A diagnosis of arteriosclerotic heart disease with coronary arteriosclerosis, occlusion with myocardial infarction and myocardial insufficiency was made. Because of the presence of a precordial murmur similar to that often encountered in congenital interventricular septal defect and the electrocardiographic findings of septal infarction, it was believed that a spontaneous perforation of the infarcted septum had occurred.

An x-ray film of the chest taken with a portable machine on January 14 was reported as showing an extensive area of right-upper-lobe consolidation, with mediastinal displacement to the right.

On the 4th day a systolic thrill was reported as present over the left third and fourth intercostal spaces. The murmur was described as loud, blowing and systolic and heard best in the fourth left intercostal space at the sternum. The hospital course persisted downhill, with sudden death on the 15th day.

At post-mortem examination† the heart weighed 360 gm. There was slight hypertrophy of the left ventricular wall. On section this revealed an old fibrotic infarct of the lower anterior wall, measuring 4.0 cm. in diameter, that also involved a portion of the anterior segment of the interventricular septum. The septum had a perforation approximately 2 cm. from the apex, extending from the anterior wall. The borders of this perforation appeared to have undergone re-epithelialization. Around the border of the septal perforation was a zone of myocardium measuring 1.5 to 2.0 cm. in thickness; it was yellowish and rather soft in consistence, appearing to be fresh compared to the left ventricular infarct. The coronary arteries showed a diffuse marked atherosclerosis, especially in the left anterior descending artery. This appeared practically occluded at two points, one 1.5 cm. and the other 2.0 cm. from the point of origin, by either extensive atheroma or old occlusion with recanalization (Fig. 5).

The pathological diagnosis was atherosclerotic heart disease, consisting of coronary sclerosis, severe, with occlusion of the left anterior descending artery, myocardial infarction of the left ventricle, anterior apical portion, old, and of the interventricular septum, fresh (5 weeks?) and perforation of septal infarct.

Figure 5. *Appearance of the Heart in Case 4. Note the epithelialization of the perforation (arrows on the right). The arrows on the left indicate an old infarct.*

Discussion

Rupture of the walls of the left ventricle is far more common than rupture of the septum. However, it has been shown that perforation of the interventricular septum is found only in the presence of severe coronary arteriosclerosis, the infrequency of septal rupture being ascribed to its rich anastomotic blood supply.[7] Sager[8] found that only 3 per cent of myocardial ruptures occur through the septum.

Most of the reported cases have had demonstrable coronary-artery occlusion, and all have had an area of infarction through which the rupture occurred. Most often, the septal involvement has been part of an anterior-wall infarction, although cases with posterior-wall infarction have been reported. The anterior wall was involved in Cases 1 and 4, and the posterior in Cases 2 and 3. In an unreported case[8] observed by one of us (M. J. N.) the posterior wall was also involved.

Usually, the perforation is single and small, but multiple communications have been noted. As many as four in one septum have been found.[9] The perforation is usually present in the lower end of the septum adjacent to one of the walls so that the auriculoventricular block, which may be seen with involvement of the upper septum (as in congenital septal defects, abscesses of the septum and metastatic lesions), does not occur. Despite ex-

*Performed by Dr. L. L. Lukash (No. A-47-711).
†Performed by Dr. Leon Morgenstern (No. A-48-54).

pectations to the contrary, intraventricular block of different degree has not been commonly encountered. Only 3 reported cases have displayed a disturbance in intraventricular conduction.[10-12]

Edmondson and Hoxie[13] report that the average time of rupture is approximately seven days after the acute infarction and that 78 per cent of the cases occur between the third and twelfth days. In 98 per cent of their reviewed cases rupture occurred during the first sixteen days of infarction. In the cases reported above, the perforation took place on the sixth day while the patient was under observation in Case 1, and probably on the third day after infarction in Case 2, presenting on admission the clinical syndrome of rupture. Case 3 was undiagnosed clinically, and in Case 4 the rupture probably occurred at some time (several weeks) prior to death since at autopsy the aperture was found to be undergoing epithelialization.

Rupture through the septum often results in a speedy death although not as quickly as in nonseptal rupture of the myocardium. All the patients in the cases reviewed by Sager[3] died within ten days. Only 7 patients in the reported cases in the literature have survived for more than one month. Three of our patients expired shortly after the estimated time of rupture. In a reported case 1 patient survived for approximately five years.[10]

Perforation of the interventricular septum is usually ushered in by a dramatic deterioration in the condition of the patient, although the time of the rupture may not be noticed. There may be pain, and there is usually peripheral circulatory failure and the rather abrupt appearance of, or increase in, the signs of failure of the right side of the heart. There is often associated nausea, vomiting and abdominal tenderness. Cyanosis, dyspnea and tachycardia may suggest pulmonary embolism; however, when the communication is small, there may be little effect on the cardiovascular dynamics. The most striking clinical feature is the appearance of a murmur known to be typical of interventricular septal defect. The murmur is often loud and harsh. It is systolic in time, is often accompanied by a thrill and is usually located to the left of the lower end of the sternum. The intensity of the murmur depends in a large measure on the size of the rupture and the general state of the cardiac dynamics. It is possible, therefore, for a murmur not to be audible especially if the defect is large. In 3 of the cases reported above, despite severe shock, the murmur characterized the auscultatory findings. This is in accord with Sager's[3] statement that the murmur is usually well marked despite the patient's poor condition. The accompanying thrill may or may not be present. Very rarely a diastolic component may be heard. The systolic bruit may be transmitted to the axilla. It is important to differentiate the murmur from that of aortic stenosis, mitral insufficiency and the rare murmur associated with ruptured chorda tendineae or papillary muscle. In the last two the murmurs are frequently more bizarre and often diastolic. Use of the precordial leads has aided considerably in the recognition of septal infarction. Dressler and Roesler[14] assert that the Q-3 T-3 pattern in the limb lead, as well as significant changes in the right precordial leads, is diagnostic of septal infarction.

Because of the added strain on the right side of the heart, the picture of myocardial insufficiency when perforation occurs is dominated largely by the phenomena of right-sided failure. The electrocardiogram may show right-axis deviation. The occurrence of a classic Bernheim syndrome has been stressed on several occasions. In fact, it is often the appearance of rapidly progressive right-sided heart failure that arouses suspicion of an altered state of circulatory dynamics.

The diagnosis of interventricular septal rupture following myocardial infarction can be readily made when the clinical or electrocardiographic findings, or both, suggest myocardial infarction involving the septum, in a patient in whom the presence, or the sudden appearance, of the typical harsh systolic murmur over the lower precordium associated with shock and often with right-sided heart failure, is noted. One must rule out possible myocardial infarction in a patient who is known to have had a congenital interventricular septal defect or an aortic stenosis. In addition, the other causes of septal perforation, such as septal abscesses, ulcerated bacterial endocarditis and septal aneurysm, must be considered. Rupture of a papillary muscle or chorda tendineae can usually be ruled out by the more frequent occurrence of bizarre diastolic murmurs and associated left-sided rather than right-sided heart failure. Where available, catheterization of the right side of the heart is likely to be of diagnostic significance. It is unlikely that Diodrast visualization of the cardiac chambers would be of any value, owing to the flow of blood from the left to the right ventricle.

Summary

Four cases of acquired interventricular septal defect due to rupture of an infarction of the septum are presented. In 3 the clinical diagnosis was made ante mortem and confirmed at autopsy. The clinical syndrome is discussed.

We are indebted to Dr. Alfred A. Angrist, pathologist, Queens General Hospital, for access to the post-mortem data and photographs, and to Mrs. Lili Rohlin for her aid in the preparation of the paper.

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AS OTHERS SEE YOU!*

Claude M. Fuess, Ph.D., Litt.D., Ll.D. (Hon.)

According to Boswell, Dr. Samuel Johnson had "in general a very peculiar pleasure in the company of physicians"; and in this respect, although in few others, I resemble the great lexicographer. George Bernard Shaw, on the other hand, once wrote, "Doctors are just like other Englishmen; most of them have no honor and no conscience." But in spite of this cynical opinion, I have found doctors, after some rather intimate experiences with them, to be the most enlightened, the most high-minded and unquestionably the most refreshing of professional men. They have even admitted this themselves, quite confidentially and, of course, modestly, in the privacy of the nineteenth hole. President Wheelock, of Dartmouth College, uttered in 1798 a famous prayer, which ran, "O Lord, we thank Thee for the Oxygen Gas; we thank Thee for the Hydrogen Gas; and for all the gases. We thank Thee for the Cerebrum; we thank Thee for the Cerebellum; and for the Medulla Oblongata. Amen!" I have found difficulty in restraining myself from praying, "O Lord, we thank Thee for the anesthetist and the radiologist and the pathologist, and, above all, for the 'ilamides' and 'mycins.'" It was, therefore, a distinguished honor, as well as a grave responsibility, to be asked to address your medical society. I shall have to trust to your tolerance — and your traditional courtesy.

Although my immediate family has never produced a physician, I once in my boyhood aspired to become one. I possessed, I thought, some very important qualifications: the desire, the enthusiasm and a passionate interest in the dissection of dead cats. But it was soon discovered that I lacked one minor desideratum. I was so clumsy with my fingers that I could hardly tie my own shoestrings. That thwarted my ambition, but I have since enjoyed some prestige in surroundings where I am usually addressed as "Doc," a salutation that gives me the same reflected glory as that enjoyed by a Kentucky colonel. Some years ago, at the Myopia Hunt Club, the golf professional called me aside and in a stealthy whisper said, "Doc, would you mind looking at a festering foot?" A little startled, I told him that, although a festering foot was not my ideal of aesthetic beauty, I should be glad to gaze on his, if that would please him, and then I found that I was expected also to bandage and prescribe. At this point one of the more discerning caddies yelled, "Hell, that ain't no real Doc!" He was absolutely right. But for a plain citizen, who hardly knows a *fibula* from a *fistula*, I have been in some disconcerting situations — enough to realize that a physician must be on call anywhere, any time, even when he is teeing off!

An elderly friend of mine, only too well acquainted with the basic differences between Scotch and rye, found himself gradually growing deafer and finally consulted an aurist, who advised him to buy a hearing aid and also to "cut out the booze." The old codger departed, apparently reconciled to the deprivation. A few weeks later, however, the doctor met him on the street, as deaf as ever and with a distinct aroma of whiskey on his breath. "What's the matter, Bill," bellowed the physician. "Why didn't you follow my advice?" "I did for a while, Doc, honest I did," was the stuttered reply. "But what I d-d-rank was so much more interesting than what I heard that I made up my mind I'd rather be deaf!"

My association with medicine men began in my childhood in an isolated village in the Mohawk Valley — not with eminent specialists but with an old-fashioned general practitioner named T. Z. Jones. The initials stood for Tobias Zacharias, but he was known throughout the countryside as "T. Z." I have vivid memories of looking out my bedroom window in January and seeing him wrapped in robes driving his open sleigh through the snowdrifts, the bells jingling merrily to announce his arrival. Hitching his horse, he would cover him with a blanket and enter wearing a shaggy pony coat and a fur cap shaped like those in the pictures of Robin-

*Presented at the annual dinner of the Massachusetts Medical Society, Boston, May 17, 1950.

son Crusoe, with tiny icicles hanging from his beard. He would warm his hands at the soapstone stove before coming into my room to feel my flushed cheek and take my pulse. I was better, of course, the minute he arrived, for although he had been on the road since dawn, he exuded quiet confidence and courage. The examination seldom took long, for he knew almost at a glance that I was suffering from my customary seasonable abscessed ear. He would advise my mother to heat me a hop bag to allay the pain. Then asking for "some water in a glass," he would distribute with his long slender fingers a mysterious white substance into little papers, which he folded with the delicate dexterity of a magician. Pouring one of the powders into the tumbler, he would say, "A teaspoonful every two hours," and handing me solemnly a peppermint lozenge, he would be off into the Arctic weather, his immediate duty done, ready to attend a birth or a death. When I acquired typhoid fever one summer, he came twice a day, and once, with the aid of my nurse, he put me into our zinc-lined bathtub packed with ice to lower my temperature and nearly lowered me into a premature grave.

Those were the primitive days when even the great Osler could write about another scourge of humanity, "Pneumonia is a self-limited disease, and runs its course uninfluenced in any way by medicine. It can neither be aborted or cut short by any known means at our command." "T. Z." had no penicillin or aureomycin in his black bag, or any x-ray apparatus or cardiograph to guide him; his diagnoses and his drugs were almost the same as those of Galen; but he understood practical psychology, and that was more than half the battle. I am sure that he did not know Sir Thomas Browne from Sir John Falstaff, but he followed Browne's classic dictum, "No one should approach the temple of science with the soul of a money-changer." And he had learned the secret revealed by William James, "The great use of a life is to spend it for something that outlasts it!" That is why his former patients still put flowers on his tombstone.

I have named Dr. Osler, and shall mention him more than once as I go along. In the summer of 1909, as a suckling scholar, I went to Oxford, intending to study in the Bodleian Library. When I presented myself to Dr. Nicholson, the librarian, with my credentials, I told him that I was investigating English satire and had my degree of A.M. from Columbia. "You mean your M.A.," said he. "No," I replied, "That isn't what they called it in America!" "Well," he growled, "if you are such a fool as not to know that your degree is an M.A., you don't deserve the privileges of this library." Back I went to the hotel — a saddened and discouraged youth, ready to sail back home.

The next afternoon I went with a friend to call on Sir William Osler, then Regius Professor at Oxford, at his residence at 13 Norham Gardens. I was only twenty-four years old, timid by nature and certainly very much flustered at the prospect of meeting a great man. He was sixty, at the height of his international reputation — an erect figure, with most impressive drooping moustachios, a wing collar, a receding forehead and very brilliant dark eyes. He received us cordially, and soon I was listening spellbound as he displayed his wonderful collection of Walt Whitman, smoothing the volumes affectionately as he told me how he attended Whitman in 1886. He asked me why I was in Oxford, and soon I found myself describing my grim experience with the guardian of the Bodleian Library. "Why," he burst out, "I'm one of Nicholson's bosses. He ought not to treat you like that." I learned then that Osler was not only *ex officio* a curator of the Library but also a member of the standing committee, which met there every Friday afternoon. "You come with me, young fellow, tomorrow morning," he said, "and we'll fix that old fossil!" The next morning I called again at the Osler home, and he walked with me to the Library. Striding straight into the lair of the Library watchdog and up to his desk, he said, "Dr. Nicholson, I want to introduce a young friend of mine who wishes to study here." The inhospitable crab of the day before smiled blandly, shook my hand as if I were president of the Royal Society, and responded, "Certainly, sir, we'll do everything in our power to facilitate the gentleman's researches." From that moment, whenever I crossed the sacred threshold during my visit, the Librarian literally dogged my footsteps, — whether I was A.M. or M.A., — asking anxiously whether I was getting the service I required. Never did contempt change more quickly to obsequiousness, and all through the timely intervention of a man whom I had never seen until the day before.

At the time of Dr. Osler's death in 1919, I saw a tribute to him that, in the light of my personal adventure, seemed especially appropriate:

> He advanced the science of medicine, he enriched literature and the humanities; yet individually he had a greater power. He became the friend of all he met, — he knew the workings of the human heart metaphorically as well as physically. He joyed with the joys and wept with the sorrows of the humblest of those who were proud to be his pupils. He stooped to lift them up to his place of royal friendship, and the magic touchstone of his generous personality helped many a desponder in the rugged paths of life. He achieved many honors and many dignities, but the proudest of all was his unwritten title, the "Young Man's Friend."

Dr. Osler was typical of many older physicians and surgeons of my acquaintance who have been ready to assist their juniors coming up the steep road to success. It is good to be loved as well as admired, and a pat on the back from a member of the Old Guard has cheered many a toiling novice. I can only say to those of you who are elderly enough to wear the laurel crown, "Go thou and do likewise!"

As time went on and I blossomed, or degenerated, into a pedagogue, I discovered what a wise and discreet doctor can mean in a school. Boys will shy off before a clergyman and quail before a headmaster, but to a physician, if he has common sense and warmth of feeling, they will bare their souls. The school physician thus often becomes a father confessor, the repository of strange secrets, and can offer advice that a youngster will take from no one else. We happened to have at Phillips Academy in the days when I was associated with it a physician perfectly adapted to that particular job, with a disarming manner, an awareness of the difference between a sin and an indiscretion, a rich sense of humor and of proportion, and a genuine human sympathy — all of which, in combination, are rare indeed. The influence of such a doctor may counteract all the machinations of the faculty and last, for the students, long beyond their day of graduation.

You will be happy, I am sure, to hear that I have no intention this evening of referring to Senator McCarthy or Professor Lattimore or, indeed, to any current controversial figure. Rather, I should like to put on record, for the first time in public, some of my opinions as a complete outsider regarding the medical profession. You must often hear unflattering remarks from your own colleagues; indeed, one of your number warned me last week to be realistic about doctors, reminding me that on the periphery of your profession are those who degrade it — the quacks, the self-seekers, the fee-splitters, the snobs and the cutthroats. I have never been unlucky enough to fall into the hands of such pirates; therefore, I instinctively think of you in terms of eulogy, not of criticism.

Probably, I do run the risk of seeming impertinent. During World War I, I shed my blood for my country to the mosquitoes on the banks of the St. John's River, in Florida. In August, a new commanding general arrived and invited me one Sunday afternoon to go with him in his car to Pablo Beach for a dip in the ocean. On the way, in a jocular mood, he started to "kid" me about some of my alleged extracurricular activities. Finally, in an attempt to hold my own, I retaliated, "Well, General, that blonde we all saw you with at Keith's Theater last evening was no lily!" Thereupon the "old bearcat," as he was affectionately called, turned to me and said in no dulcet tones, "Fuess, sometimes I think you don't realize who I am." If any of you, after this particular hearing is over, comes up to say, "Fuess, sometimes I think you don't realize who we are," I shall resume my humble position as a past and prospective patient, and accept my squelching.

Dr. Oliver Wendell Holmes once gave some sound counsel to his students:

> Medicine is the most difficult of sciences and the most laborious of arts. It will task all your powers of body and mind if you are faithful to it. Do not dabble in the muddy sewer of politics, nor linger by the enchanted streams of literature, nor dig in faroff fields for the hidden waters of alien sciences. The great practitioners are generally those who concentrate all their powers on their business.

Holmes himself, although by no means a "great practitioner," set a very bad example to others, for eventually he was overwhelmed by his avocations. But surely the most distinguished medical men, for reasons that I do not undertake to explain are more versatile than lawyers or teachers or bankers. They have hobbies ranging from asteroids to zithers.

As for the "muddy sewer of politics," I remember Dr. Charles E. Abbott, of Andover, a truly great country practitioner, looking as Hippocrates or Vesalius might have looked, with his patrician features and huge shock of silver hair, who, when he drew near three score, was elected our Andover representative in the General Court. His name was naturally the first alphabetically on any roll call, and many of his colleagues have told me how inspiring it was to see his dignified figure rise to vote and lead the way.

In golf, I have many reasons for respecting the prowess of medical men. Once at Hobe Sound, in Florida, I formed one of a quartet with three surgical paragons. In the middle of our vacation an epidemic of influenza attacked our party, — both husbands and wives, — and no physician was in the vicinity. It turned out that the surgeons had only two palliative measures — amputation and penicillin. Each one was perfectly willing to operate, if urged, on his companions, but there was a general rejection of that type of treatment. So they fell back on penicillin, and each surgeon insisted on having a share in the job. Almost the only words I heard for about five days were "roll over," and I became so much accustomed to the command that I automatically turned face downward whenever one of them approached. Fortunately, all of us recovered, although a trifle sore on our southern exposures.

It must be mentioned to their credit that I dwelt thus among surgeons without being disillusioned. Their language in crises was more than slightly corrosive to my chaste ears, but my vocabulary has been enriched by it. Furthermore, most doctors of my acquaintance have their quota of the pleasant minor vices. It is true that Dr. Osler, in his famous address to Yale students, spoke out against smoking, saying: "That befogged, woolly sensation reaching from the forehead to the occiput, that haziness of memory, that cold, fish-like eye, that furred tongue, and last week's taste in the mouth,— too many of you know them, — I know them, — they come from too much tobacco."

This diatribe reminds one of President Neilson's classic remark to Smith College students, "Smoking is a filthy, expensive, and injurious habit, — to

which I am inordinately addicted!" But I have observed that most physicians, however much they may recommend abstinence to their patients, have their relaxed hours when they sit in a nicotinal cloud, making no effort to resist temptation.

Since the doctors of fiction are among my constant bedside companions, I have often speculated on what a picturesque group they would make on a South Pacific island or in a Saturday-night poker game. First on the list is Dr. Slop, the "man midwife" who underwent such difficulties in bringing Tristram Shandy into the world — Dr. Slop, whom Sterne describes as a "little, squat, uncourtly figure, of about four feet and a half perpendicular height, with a breadth of back and sesquipedality of belly which would have done honour to a serjeant in the Horse Guards." With him, of course, although not very congenial, would be Lydgate in George Eliot's *Middlemarch*, unquestionably the best novel ever written about a doctor's life — Lydgate, who made the colossal, irretrievable blunder of marrying a frivolous wife and thus was dragged to ruin. I should like especially to include Dr. Thorne, of Trollope's "Barchester" series, who as an elderly bachelor won the hand of the richest spinster in England. At his side would be another of Trollope's physicians, with the ominous name of Dr. Fillgrave. Dr. John Watson would inevitably be one of the company, although his professional skill was obscured by his collaboration with Sherlock Holmes. The crudest of them would be Dr. Martin Arrowsmith, the hero of Sinclair Lewis's novel in which the medical profession is slandered more outrageously than in any volume ever printed. We must not omit Stevenson's Henry Jekyll, M.D., D.C.L., LL.D., F.R.S., although few would want him around during his transmutation into the bestial Mr. Hyde. To these might well be added, if only for fun's sake, R. Austin Freeman's amazing Dr. Thorndyke, the cleverest detective of them all, who apprehended his criminals through the use of medical science and solved the perplexing case of Oscar Brodski. Put these figures around any table, with the port flowing freely and your toastmaster acting as a foil, and the conversation would be worth recording.

But we do not need to go to the doctors of fiction to find stimulating company. There is always the "choir invisible of those immortal dead who live again in minds made better by their presence" — the doctors who have wandered into other fields. Think, for example, of Sir Thomas Browne, author at thirty of the brilliant but exasperating *Religio Medici*, the bachelor who wished that human beings could procreate like trees and also in his rashness called woman "the rib and crooked piece of man." For his sins he was married four years later and had ten children, having presumably modified his earlier philosophy. One thinks naturally of Dr. Oliver Goldsmith, with his ridiculous excursions into natural history, who maintained until his death that he chewed food by moving the upper jaw. Then there are Rabelais and Keats, the two greatest of literary physicians. It was Keats who passed his examination as apothecary, but abandoned surgery when, while opening a patient's temporal artery, he found his imagination wandering into the realms of gold. He later wrote, "On reflecting what passed through my mind at the time, my dexterity seemed a miracle, and I never took up the lancet again." Another physician, Dr. Garth, wrote what is unquestionably a strong candidate for the dullest poem ever written, *The Dispensary*, guaranteed to be more efficacious than phenobarbital as a means of producing quick slumber. John Locke, the philosopher, was also a physician and left behind a remarkable record of the progress of a case of hydatid cyst of the liver; so too was Smollett, the novelist, who functioned as a ship's surgeon. Nearer our own time, some of us cannot have forgotten Dr. S. Weir Mitchell, the Philadelphia neurologist who wrote *Hugh Wynne*, *Free Quaker* and also a popular treatise entitled *Wear and Tear*, in which he called attention to the inability or indisposition of Americans to play, and to the increase in nervous disorders that inevitably followed. After reading this illuminating book, I found that my conscience was much less sensitive regarding billiards or Canasta. I cannot neglect Dr. David Livingstone, the explorer, who was found dead kneeling in prayer by the side of his cot in the interior of Africa. And I must pass over, with a bare reference, Dr. John Browne, of *Rab and His Friends*, Drs. Trudeau and Grenfell with their fascinating autobiographies, Dr. Richard C. Cabot, with his *What Men Live By*, and Dr. Hugh Young, with the racy, uninhibited chronicle of his adventures. Many of them have had the gift of phrasing — especially those two masters of our own period, Dr. Osler and Dr. Cushing, who blended medicine and literature as few others since Dr. Holmes have done. And no catalogue would be complete without mention of Dr. Albert Schweitzer, that genius in triplicate, who is not only a doctor but also a theologian and a musician. It is indeed a noble company who have brought, and are bringing, honor to your profession.

It is a truism that the chief discernible progress toward civilization in our time has been made through applied science. The Greeks, the men of the Renaissance, were our superiors in the fine arts, and we have been unable to equal them. But in engineering and bacteriology and sanitation and surgery we have gone far beyond anything they ever dreamed of. In the eighteenth century, in the days of *Gil Blas*, medicine was still a matter largely of cuppings and bleedings and purgings and blisterings. Dr. Holmes said, in his early days as a practitioner, that the physician was like a watchmaker having charge of timepieces that he could not open; he must make the best guess he can. I remember seeing in the cloisters of Winchester College, in

England, the long row of tablets erected in memory of poor little boys who died at that school because of insufficient care and inadequate medical treatment. Modern diagnosis and curatives would have saved millions of potential Miltons and Lincolns.

Sometimes the physician or the surgeon has been able to affect the course of history. In the summer of 1893, at a crucial moment in the financial situation of the United States, President Grover Cleveland had to undergo a serious operation for sarcoma in the roof of the mouth. If it had become known that he was ailing, the bottom would have dropped out of the stock market, for he, and he alone, could keep a group of Congressional radicals from forcing this country off the gold standard. It was announced from the White House that the President was taking a short cruise, and the operation was performed secretly by Dr. Joseph D. Bryant, on the yacht *Oneida*, as it steamed slowly up the East River. Fortunately, no Drew Pearson or Walter Winchell learned about it, and the public was kept in entire ignorance until 1917, long after Cleveland's death. Dr. William W. Keen, of Philadelphia, who assisted Dr. Bryant, said later that on the surgeon's instruments — and nerve — depended not only the life of a human being and of an illustrious ruler "but the destiny of a nation." A century before, according to him, nothing could have been done.

In May, 1906, Woodrow Wilson, then president of Princeton, after suffering a hemorrhage of the blood vessels of the eye, was told by two famous American specialists that he had arteriosclerosis and must give up everything and henceforth live a quiet and retired life. He went to Europe and there met a Dr. Boyd, who advised him that it would be better for a man of his temperament to go back to work than to spend aimless and anxious years until he was overtaken by death. He was then only fifty, and all the major accomplishments of his career were ahead of him. But for wise medical attention, with reliance on recently discovered sedatives, he could never have achieved what he did.

Dr. Osler resolved, early in his apprenticeship, to fight what were then three sinister afflictions of mankind: typhoid, tuberculosis and pneumonia. He lived long enough to see the two first brought under control, and although it was the pneumococcus that caused his death, even that infection was, within a quarter of a century, much less of a menace. So it is, of course, with smallpox, yellow fever and other forms of pestilence. We may yet, through the wonderful persistence of your research workers, reach the situation described in Samuel Butler's *Erewhon*, a community in which ill health was regarded as a crime and a man accused of "pulmonary consumption" was convicted and sentenced to imprisonment, at hard labor, for the rest of his miserable existence. Some of my friends were discussing the other day how they would prefer to die. One of them said, "As for me, let me be shot by a jealous husband at the age of ninety-three!" If you gentlemen persevere in your miracles, that may be the fate of many a virile citizen.

On matters of scientific import, I am, of course, really unqualified to speak. A clergyman, presiding at the funeral of one of the community's "crusted characters" and wishing to emphasize the essential vitality of the human soul, looked down at the open coffin and declaimed solemnly, "My friends, this is not our real neighbor who lies here before us. The shell is with us, — but the nut is gone!" His phrasing was not felicitous, but he meant well. And so I may, perhaps, be pardoned if I say a word, not on the actual accomplishment, which you yourselves know so much better than I, but on the spirit in which the work has been started and carried on. The men and women who have devoted themselves to research, endangering and even losing their lives in the quest for remedies, are among the heroic members of our race, but with them have gone the doctors who have profited by the discoveries and given themselves, as many of you have done, to the direct alleviation of suffering. Robert Louis Stevenson, in his well known dedication to his *Underwoods*, paid a deserved tribute to the whole army of medical men who have made this a more tolerable world:

> There are men and classes of men that stand above the common herd; the soldier, the sailor, and the shepherd not infrequently; the artist rarely; rarelier still, the clergyman; the physician almost as a rule. He is the flower (such as it is) of our civilization; and when that stage of man is done with, and only remembered to be marvelled at in history, he will be thought to have shared as little as any in the defects of the period, and most notably exhibited the virtues of the race. Generosity he has, such as is possible to those who practice an art, never to those who drive a trade; discretion, tested by a hundred secrets; tact, tried in a thousand embarrassments; and what are more important, Heraclean cheerfulness and courage. So it is that he brings air and cheer into the sick-room, and often enough, though not so often as he wishes, brings healing.

The supreme irony of history is that while man, in one mood, is laboring through his ablest representatives and from the noblest motives to relieve pain and prolong life, he is also, in another mood, toiling simultaneously and with equally tireless energy to produce more effective instruments of annihilation. It is indeed tragic that while laboratories are being equipped for the elimination of cancer, millions of dollars are also being spent to concoct a bomb that will increase misery. At the very moment when we seem to be ready to market a drug that will at least arrest and may possibly cure arthritis, the nations of the world are experimenting with the means of crippling the finest youth of the race. Healing on the one hand, killing on the other — these are going on side by side. It seems a pity that man, so noble in reason, so infinite in faculty, in action so like an angel, in apprehension so like a god, cannot better regulate his own affairs.

When I was once emerging from the fumes of ether after an operation, I looked up and, seeing an

attractive nurse's face close to mine, said to her, in the language of the Book of Books, "Thou hast dove's eyes!" She fled in terror, thinking that she had a madman as a patient, and refused to appear again. But my tribute to her was heartfelt, as it is to my physicians, indeed to all physicians. Socrates, before swallowing the fatal hemlock, said to Crito, "I owe a cock to Aesculapius." I am certainly no Socrates, but I feel that we owe a vast debt to Aesculapians!

For their patience with the stupid and the cowardly, for their quiet devotion to the inevitable truth, for their constant courage and unquenchable hope, for their cheerfulness even in the darkest hours, for their faith in humanity even when they see it at its worst, for what they have sacrificed and what they have forgiven, I for one am deeply grateful.

Dr. Osler, in the inspiring address from which I have already quoted, outlined for Yale students a way of life, stressing the necessity of living for the day only and for each day's work: "Life in Day-Tight Compartments." Personally, I prefer to do a little planning for tomorrow and for the day after tomorrow, and I like better Dr. Livingstone's slogan, "Fear God and work hard!" But that is aside from the point. Dr. Osler, toward his conclusion, emphasized the advice of Jesus to Nicodemus, "Ye must be born of the spirit!" That is the secret of enduring greatness, in any occupation, and not the least of all, in medicine. Stephen Paget phrased it perfectly when he said, "If a doctor's life may not be a divine vocation, then no life is a vocation, and nothing is divine."

I have tried to pay a long-standing debt, and I only wish that it could have been done in winged words instead of faltering ones. But however crude the sentences may have sounded, they have the single merit of sincerity. To your presidents, old and new, all honor, and as for your society, *Vivat, Crescat, Floreat in Aeternum!*

THE CAST SYNDROME*

Review of the Literature and Report of a Case

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THE purpose of this paper is to call attention to the dangers of pernicious vomiting in connection with the application of a body cast. Cases of acute gastric dilatation abound in both textbooks and periodic literature, but there is remarkably little material concerning the application of a body cast as a cause. No detailed description of acute gastric dilatation (gastrectasia) is given, but a brief background is offered.

Acute gastric dilatation was first mentioned by von Rokitansky[1] in 1861, and his theory of its etiology still holds. He believed, and his theory is substantiated by Conner[2] and others, that the essential process is due to obstruction in the third portion of the duodenum, probably because of an arteriomesenteric compression. Borchgrevink[3] on the other hand, ascribed the condition to primary gastric paralysis causing direct pressure on the duodenum in its passage over the spine or to secondary arteriomesenteric compression induced by distention of the stomach with pressure on the duodenum. Modern tests[4, 5] still cite these two theories as the basis for the etiology of this condition, and Dragstedt[6] supports the theory of a nervous reflex as the cause in the production of gastrectasia. However, the exact mechanism remains obscure, and the chief problem is whether dilatation of the stomach precedes mesenteric obstruction of the duodenum or vice versa.

Conner's[2] etiologic classification is still adhered to in present-day reports of acute gastric dilatation. He divides the cases into five groups: convalescent patients recovering from severe and wasting diseases; cases occurring after back injuries; those occurring after indiscretions of diet (overeating); those with deformities of the spine; and all idiopathic types. It is of interest to note that the classification is the only one mentioning gastrectasia in association with the application of a body cast. The case presented below is common in that it deals with acute gastric dilatation, but unusual because it was precipitated by a body cast.

CASE REPORT

An 18-year-old girl was admitted to the hospital on June 26, 1949. The past medical history was irrelevant. The patient had been thrown from the handle bars of a motorcycle, sustaining a compound fracture of the lower third of the left femur. She was put in Russell's traction for 2 weeks; to immobilize the femur, a body cast (hip-spica type) was applied on July 26. Three days later the cast over the abdomen was loosened because of vomiting and pain occasioned by direct compression of the cast. The patient was discharged in good health on July 29.

She was readmitted to the hospital on August 9 with a diagnosis of gastroenteritis. The history revealed that she had experienced recurrent periods of vomiting, and that there had been pressure on the abdomen. She had been unable to eat well and had voluntarily restricted fluids; all stools had been formed, and there had been no fever or diar-

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rhea. During the night before admission she had again begun to vomit, and not being able to stop had been admitted to the hospital.

Physical examination was negative except for apparent body-cast compression. On August 8 a portion of the cast over the abdomen was cut out, giving much relief to the patient; however, on the following day she continued to vomit every few hours so that a Levine tube was passed, with relief. At that time all laboratory studies were negative. She improved and was sent home on August 12 with the tube removed.

At home, according to the history obtained from her mother, she was well until August 16, when unexplained vomiting again began. At first she tolerated small amounts of food; however, later she could scarcely retain anything taken by mouth. This continued, the vomitus consisting of bile and mucus. Urinary output was fair during this period. The patient became comatose on the trip to the hospital, where she was admitted unconscious on August 24, at 12 p.m.

At that time she was found to be cyanotic and comatose, frothing at the mouth and hyperpneic; the skin was cold and clammy. Chvostek's sign was positive, and rigidity was present. The body cast had not been removed. The blood pressure and pulse were not obtainable; the temperature was subnormal. The diagnosis was acute alkalosis. Oxygen was given, and fluids consisting of a total of 800 cc. 5 per cent glucose in water, 6 units of plasma, 500 cc. of blood, 2000 cc. of physiologic saline solution and 500 cc. of 5 per cent saline solution were administered intravenously up to the time of death.

At 1:15 p.m. the blood pressure was 60/0; the temperature was above the level of the thermometer. Alcohol baths were started. At 2:00 p.m. blood could be drawn for study for the first time. The carbon dioxide combining power was 79 vol. per cent, and the plasma chloride 260 mg. per 100 cc. At 3:00 p.m. the cast was removed; the temperature was 108.4°F. The patient was soaked in ice and alcohol continuously. At 5:15 the temperature was 102°F., the blood pressure 60/0, and the pulse 150. Despite all measures taken the patient died at 5:37.

Autopsy revealed marked edema of the lungs, accompanied by myocardial degeneration. The stomach was dilated to the approximate size of a small watermelon and contained liquid and gas. The mucosa showed scattered, red telangiectatic markings. The entire duodenum was dilated up to the ligament of Treitz; at that point, there was abrupt reduction in the diameter of the small intestine, whereas distally the entire intestine was normal in diameter. There was no evidence of an organic obstructive lesion. The diagnosis was acute massive gastric dilatation, with massive pulmonary edema following application of a body cast for a compound fracture of the left femur (cast syndrome).

Discussion

This case is the only one of its kind in the records of this hospital; however, a similar situation must have been met with many times but without the recognition of association of gastric dilatation with a body cast. Patients in body casts often require decompression by means of a Levine tube, but they usually recover within twenty-four hours without residua. Another case of a cast syndrome was recently observed at Temple University Hospital in Philadelphia.[7] A twenty-year-old woman who had been placed in a body cast for a lumbar injury had a similar course ending in death. The autopsy findings showed acute dilatation of the stomach and small intestine up to the splenic flexure. (This case has not yet been reported.)

In a review of the literature on the cast syndrome only 4 cases were found. In the first of these, reported in 1878 by Willett,[8] a seventeen-year-old patient with a kyphotic spine was placed in a body cast (Sayre's body jacket). At home vomiting continued even after the cast had been removed, and the patient died in forty-eight hours. Autopsy showed a dilated stomach occupying half the abdominal cavity. There was no intestinal engorgement, and no obstruction was found.

In the case reported by Buzzard[9] in 1880 a twenty-two-year-old man with Pott's disease was put into a body cast. Six days later he ate a hearty meal, after which he complained of discomfort. On the next day vomiting began, continuing throughout the night. The cast was removed, but the patient died that evening with acute abdominal distention. Autopsy revealed a "kink" in the duodenojejunal junction, with acute distention of the stomach and duodenum. Buzzard postulated that the cause of death was pressure on the third part of the duodenum between the superior mesenteric artery and the spine. On the basis of other cases he was familiar with at that time he believed that a third of all acute cases of gastrectasia are due to obstruction of the duodenum by the mesentery.

In 1900 Kelling[10] reported the case of a sixteen-year-old girl with a congenital lumbodorsal scoliosis who was placed in a body cast from neck to trochanters. Two days later vomiting began after a heavy mid-day meal. On liquids the patient continued to vomit bile and was put to bed. Vomiting continued off and on until she had oliguria, abdominal distention and cyanosis. There was no passage of gas or feces. A window was cut in the cast, with much relief, and she began to take fluids. On the next day she vomited again, and the cast was removed, with the presenting symptoms of cyanosis, weak pulse, pain in the abdomen and thirst. The patient went into shock associated with enormous distention of the abdomen. A tube was inserted, and 3 liters of liquid was aspirated while clysis was begun. On the next day she was able to take liquids and improved. After a total illness of two weeks she recovered, subsequently regaining 20 pounds of weight that she had lost. The similarity between Kelling's case and the others is noted, but the cast was removed early enough for recovery.

Conley and Miller,[11] in 1935, discussed the case of a fifteen-year-old boy who was put into a Bradford frame because of an injured spine incurred from a fall. Because of persistent pain, a cast (body and neck) was applied and the patient discharged. He was seen twice thereafter and was found to be perfectly well. About six weeks later he was admitted to the hospital because of pain, a sensation of tightness in the abdomen, vomiting, obstipation and abdominal distention. Through a window cut in the cast, cyanosis, with edema of the abdominal wall, was noted. The symptoms persisted, and a Levine tune, with suction, was instituted for four days and then discontinued. A barium swallow showed a tremendously distended stomach, necessitating reinsertion of the tube. Parotitis and septicemia (temperature of 107°F.) developed, and the patient died eight days after admission. Autopsy

disclosed a markedly dilated stomach with a perforation in the fundus near the diaphragm. Pericardial and chest fluid proved the organism to be *Escherichia coli.*

In the majority of cases presented it is apparent that the presence of a body cast was not appreciated as a factor in the production, aggravation and sequelae of acute gastric dilatation. Regardless of the precautions taken to mold a cast, it is almost impossible not to distort the anatomy of the spine, because the cast does not allow for normal soft-tissue expansion and retraction. The nature of the ensuing mechanism is still problematical, but the end result can be fatal. The time to remove the cast varies with each case; the balance between health one day and shock with potential death the next is a precarious one. Consequently, the greatest care must be exercised in the treatment of patients in body casts who present the symptoms of persistent vomiting and gastric dilatation. This precaution consists of immediate gastric intubation, removal of the entire cast, if necessary, and strict regulation of body fluids as indicated from laboratory and clinical findings.

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IMMUNE RESPONSES AND REACTIONS TO DIPHTHERIA AND TETANUS TOXOIDS, WITH PERTUSSIS VACCINE, ALUMINUM PHOSPHATE PRECIPITATED

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IMMUNIZATIONS combining diphtheria and tetanus toxoids with pertussis vaccine, using alum or aluminum hydroxide as an adjuvant, have been reported in studies by di Sant' Agnese,[1] Volk,[2] Fleming[3] and others. Holt[4] has described the preparation of a purified diphtheria toxoid with aluminum phosphate as the mineral carrier. Clinical trials of this material have been extensive.[5] We agree with Holt[4] "that aluminum phosphate is an extremely suitable vehicle for adsorbing diphtheria toxoid when used for human prophylaxis, in that local or general reactions were absent or trifling."

This study presents the use of a new product in the sense that aluminum phosphate has not been used previously as an adjuvant in a biologic preparation containing tetanus toxoid. Animal tests showed high antigenicity, but because of the lack of evidence regarding its adjuvant action with tetanus toxoid in children, this study was undertaken. Also presented briefly are the reactions and the small amount of information obtained on the immunizing ability of the other two components. No preimmunization titers were determined, so that the exact status of the children is not known regarding diphtheria

Table 1. *Reactions.*

Injection	Total No. of Injections	Percentage with Local Reactions							
		Erythema				Infiltration			
		0	2.5 cm.	2.5–5 cm.	5 cm.	0	2.5 cm.	2.5–5 cm.	5 cm.
First (0.5 cc.)	113	45	30	20	5	80	11	6	3
Second (0.5 cc.)	87	42	30	20	8	79	12	6	3
Third (0.5 cc.)	87	53	27	14	6	79	17	1	3
Booster (0.3–0.5 cc.)	134	57	13	13	17	72	16	6	6

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and pertussis before immunization. As these were primary immunizations against tetanus, it can safely be assumed that there was no immunity against tetanus in these children previous to immunization.

Plan of Study

The product used was prepared by the Massachusetts Department of Public Health, Division of Biologic Laboratories. The diphtheria and tetanus components were purified and concentrated by ammonium sulfate fractionation. The pertussis vaccine was prepared from Phase I organisms grown on Cohen–Wheeler fluid medium and standardized at 20,000,000,000 organisms per cubic centimeter. This material was furnished to physicians, clinics and institutions who agreed to report the reactions, using a special form. Efforts were made to obtain bloods one month after the last injection, whenever possible.

Titrations on these bloods were carried out at the laboratory. The diphtheria antitoxin titrations were done in rabbits, the Römer[6] intradermal test being used. Titrations for tetanus antitoxin were done in guinea pigs according to the method recommended by the National Institutes of Health.[7] The serum agglutinins against *Haemophilus pertussis* were determined by a procedure similar to the method described by Flosdorf[8] except that the vaccine was prepared from fluid rather than Bordet-Gengou solid mediums.

Method of Injections

The circular accompanying each vial advised three *intramuscular* injections of 0.5 cc. each at four-week intervals. As only one "antigenic cyst" occurred after injection, it is believed that for the most part this instruction was followed. The importance of intramuscular injection has been stressed by many and recently emphasized by Sauer,[9] whose recommendations are as follows:

> Alternate lateral gluteal areas (starting with the left proximal area) are preferred sites for the administration of alum precipitated antigens in children under three years of age. Needles (12 mm., 25 gauge) and syringe (1 cc.) are cleansed in distilled water, dried and sterilized in an oven at 160°C. for one hour. The child is held firmly to prevent squirming. The needle does not deviate from its original course. Each deeply administered dose is terminated with 0.1 cc. of air. The needle remains in place for a few seconds before it is quickly withdrawn. The site is immediately massaged gently with sterile gauze. Subsequent doses are never administered near the site of a previous injection. Occasionally a deep circumscribed nodule may be palpated for a month or longer, but abscess has been almost completely eliminated.

Sauer and others also recommend that children with a tendency to convulsions be omitted from any immunization against pertussis.

Report of Reactions

Reactions were reported on forms provided. It was intended whenever possible to have the parent make these observations. The lack of reactions reported from the larger clinics in many cases indicated to us only that they were busy clinics and that the cards were not often given to the parent. In a total of 765 injections 583 children were recorded as having no erythema and 708 as having no infiltration.

In an effort to assess more accurately the incidence and degree of local and general reactions the reports of patients of private physicians and the smaller clinics were separated and summarized (Table 1). In these reports the mother for the most part indicated the reactions or lack of them. The details on most cards showed careful observations.

In age distribution 40 per cent of the children receiving injections shown in Table 1 fell in the group of six to twelve months, and 23 per cent were four years and older. In a similar but more extensive study by di Sant' Agnese[1] mentioned above, there was a higher percentage of children six to twelve months of age and relatively few in the older group; in his study considerably less local erythema was reported. In this study, however, less infiltration, fever and other reactions followed each injection. As we anticipated, the highest percentage of larger local reactions was found in the "booster group."

Table 1 (*Concluded*).

Injection	Percentage with Fever			Percentage with Other Reactions		
	None	Slight*	High†	Irritability	Vomiting	Anorexia
First (0.5 cc.)	91	8	1	8	1‡	—
Second (0.5 cc.)	88	10	2	13	1	—
Third (0.5 cc.)	86	9	5	7	2	—
Booster (0.3–0.5 cc.)	93	4	3	7	—	2

*100–102°F.
†102–104°F.
‡1 cyst.

Immune Response

Only 49 blood samples were obtained from private patients and clinics. A total of 76 samples were obtained, including 27 from children in institutions

who for the most part were between two and five years of age. Approximately 65 per cent of the children from whom bloods were obtained were under one year of age at the time of the first injection.

The results of the tetanus antitoxin titrations (Table 2) showed 100 per cent immunity with 0.1 unit per cubic centimeter as the level indicating immunity. Small amounts of blood in 5 samples reduced the number of tests that could be completed to 71.

Diphtheria antitoxin titrations similarly showed 100 per cent immunity with 0.03 units per cubic centimeter as the level most commonly considered adequate.

Table 3 demonstrates the immunity to pertussis as judged by agglutination titers of 1:320 or over. The 75 per cent "protection" obtained is lower than that in the study of di Sant' Agnese[1] mentioned above (85 per cent). However, in comparable age groups the results are the same. We do not have an explanation for the poorer results in the older children. The group of children two years of age and under is considered the more important from the standpoint of complications from the disease. As pointed out above, the figures for diphtheria and pertussis immunity are not presented as an accurate measure of the antigenic efficiency of the triple antigen used in this study because of the lack of preinjection blood titers.

TABLE 2. *Antitoxin Titrations.*

ANTITOXIN LEVELS	DIPHTHERIA ONE MO. AFTER IMMUNIZATION	TETANUS ONE MO. AFTER IMMUNIZATION
	NO. OF CASES	NO. OF CASES
units/cc.		
>0.1	22	4
>1.0 <3.0	22	14
>3.0 <5.0	10	14
>5.0	12	39
Total cases with protective titer	66 (100%)	71 (100%)

TABLE 3. *Titration of Pertussis Serum Agglutinins One Month after Immunization.*

AGGLUTININ TITERS	PATIENTS UNDER TWO YR.	PATIENTS OVER TWO YR.	TOTAL PATIENTS IN BOTH AGE GROUPS
<1:160	0	3	3
1:160	7	9	16
Total without protective titer	7 (15.5%)	12 (38.7%)	19 (25%)
1:320	12	9	21
1:640	13	7	20
1:1280	8	2	10
1:2560	5	1	6
Total with protective titer	38 (84.5%)	19 (61.3%)	57 (75%)

SUMMARY

Reactions in a clinical study of diphtheria and tetanus toxoid with pertussis vaccine, aluminum phosphate precipitated, are tabulated. The antigen was injected *intramuscularly* in three 0.5-cc. doses four weeks apart. The reactions following these injections as well as 134 "booster" doses were not severe either locally or generally in this group of "free-living" children. The importance of proper injection was stressed to the physicians using the product.

The immunity response to the tetanus component was more than adequate in 100 per cent of the children tested one month after the last dose. As there were no previous tetanus immunizations in these children the tetanus immunity as shown by post-injection titers should be an accurate index of the immunizing ability of this antigen.

Adequate immunity was found in 100 per cent of the bloods tested for diphtheria antitoxin and 75 per cent of those tested for pertussis immunity as indicated by the agglutination tests. The limitations in interpretation of these two tests are pointed out.

We are indebted to many physicians, clinic nurses and institutional employees for the co-operation that made this study possible. The diphtheria, tetanus and pertussis titrations were carried out at the laboratory by Miss Louise Wyman, Dr. Joseph Stone and Miss Leslie H. Wetterlow.

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MEDICAL PROGRESS

SURGERY OF THE ESOPHAGUS*

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IT IS noteworthy that in the year 1950, a Medical Progress report should be concerned solely with the surgery of the esophagus — noteworthy because only fifteen years ago, Churchill[1] recalled that the esophagus had been termed one of "the last frontiers of surgery" in a discussion of the unsuccessful operations that had been performed on this organ up to that time. The surgery of that era was concerned with esophagoscopy and the removal of foreign bodies from the esophagus, bougienage for strictures and cardiospasm, the two-stage removal of diverticula of the cervical segment and some disheartening attempts to duplicate Torek's successful resection of a carcinoma performed in 1913.

Today, the contributions of the pioneers in the field, the advent of the antibacterial agents and the development of all the collaterals of surgery have made the operative mortality for most of the surgical procedures on the esophagus very acceptable and have greatly enhanced the chances for cure or palliation.

Many of the reports in the literature contain data that must be considered tentative, particularly regarding carcinoma of the esophagus, since insufficient time has elapsed in many cases for final conclusions to be adduced. Moreover, results in the patients being operated on at present with recently developed technics will not be available for critical analysis for some years.

This report concerns the following problems of the surgery of the esophagus: spontaneous perforation; trauma; diverticulum; cardiospasm; benign strictures; esophageal varices; benign tumors; and carcinoma.

SPONTANEOUS PERFORATION OF THE NORMAL ESOPHAGUS

Spontaneous perforation is a distinct clinical entity in which sudden rupture through all layers occurs in the lower end of a normal esophagus. Such a perforation usually occurs after violent retching or vomiting. Acid gastric contents and food particles are driven into the mediastinum, the left pleural cavity and, occasionally, the right pleural cavity. The resulting insult in this unique esophageal lesion is devastating to the patient. The features of the disease are distinctive and yet easily overlooked. Until recently, the diagnosis was rarely made during life so that definitive treatment could be instituted, and for this reason the mortality has been 100 per cent.

Since the lesion has been shown to be amenable to prompt surgical intervention, the diagnosis should be considered by the physician whenever there is sudden excruciating pain in the epigastrium and chest, usually after vomiting. The clinical picture may be confused with many emergency conditions, including acute coronary thrombosis, perforated peptic ulcer, acute pancreatitis, dissecting aneurysm of the aorta and spontaneous pneumothorax. Recently, Barrett[2] reported the first case of survival from spontaneous esophageal perforation treated by thoracotomy and surgical repair. Lynch[3] made the diagnosis and operated on 3 patients, with recovery. Ware and Strieder[4] reviewed the subject and on the basis of experimental and clinical studies, concluded that immediate surgical intervention offers the best hope of cure of this lesion. Kinsella et al.,[5] in a comprehensive report based on 5 cases, came to similar conclusions. If the condition is borne in mind, when a patient with a suggestive history is seen, chest roentgenograms, thoracentesis and the presence of subcutaneous or mediastinal emphysema, or both, will usually enable one to arrive at the correct diagnosis and to proceed with the appropriate therapy.

TRAUMA

During the course of instrumentation of the esophagus for diagnosis, dilatation or the removal of foreign bodies, accidental perforation may occur. The advent of the antibacterial agents has done much to lower the mortality and to reduce the morbidity of the surgical approach to these lesions, particularly when the perforation exists in the thoracic portion of the esophagus. Hitherto, the onset of fever, pain and emphysema in the tissues of the mediastinum and neck after instrumentation have sufficed to merit prompt surgical intervention by cervical or posterior extrapleural mediastinotomy, or both, depending upon the site of perforation, to establish dependent drainage of the acute mediastinitis. Adams[6] believes that gastrostomy should always be done for purposes of fluid and food administration and for rest during healing. In 4 of his 7 cases, it was the initial procedure.

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In my experience, this is not always essential but it may be an important part of the surgical plan. A soft Penrose tube introduced through the nose into the stomach may suffice to introduce fluids and food while permitting rest of the esophagus until the perforation has healed.

If symptoms of perforation occur after instrumentation at the hands of an operator of competence who has not recognized the accident during the operation and, therefore, the perforation is surmised to be tiny (a puncture rather than a laceration), a conservative policy may be adopted for a period of observation. During this period massive doses of penicillin (500,000 units every three hours) and streptomycin (0.5 gm. every six hours) should be given. With this regime unequivocal perforations have been seen to heal spontaneously without sequelae. One should bear in mind that antibacterial therapy may produce a masking effect. Periesophageal abscess may form, requiring drainage. Evidence of progression of infection demands prompt surgical intervention.[7]

In civilian life, a sharp foreign body, such as glass, bone slivers or wire, may be swallowed and perforate the esophagus. Usually, mediastinitis or localized abscess formation ensues, requiring drainage. I have, however, removed a 2.5-cm. piece of fine strainer wire, which had been ingested with apple sauce and had perforated the cervical portion of the esophagus, transversed the soft tissues of the neck and presented subcutaneously in the anterior triangle. At no time was there evidence of sepsis.

War wounds of the esophagus have seldom been treated by military surgeons, according to Sommer and O'Brien.[8] Because of the close proximity of the organ to the trachea, the great vessels of the neck and the thoracic aorta, esophageal wounds are often associated with other injuries causing sudden death. Only rarely, therefore, have soldiers with esophageal wounds reached even the most advanced medical installation. However, Sommer and O'Brien suggest that prompt surgical intervention will save the lives of some of these patients. The use of the antibiotic drugs, together with adequate and prompt drainage of mediastinal and pleural infections, constitutes the essential features of treatment. Primary closure of the esophageal wound, when feasible, should be attempted. Surviving patients may have fistulas for some time or may develop strictures, which will require dilatation.

Diverticulum of the Esophagus

Pulsion diverticulum in the pharyngocervical portion of the esophagus is relatively common, many cases having been reported. It has been demonstrated repeatedly that the surgical removal of these sacs is a feasible and safe procedure so that the opportunity of surgical cure should be offered to any patient who complains of dysphagia, regurgitation or embarrassing noises during deglutition and in whom the roentgenogram, after a barium swallow, demonstrates a diverticulum of suitable proportions. The recent literature has been largely concerned with discussions of the relative advantages of the one-stage procedure over the two-stage operation. Lahey,[9] long an advocate of the two-stage operation, believes that this technic is safer because if leakage occurs mediastinitis will not ensue as a possibly fatal complication. He has employed this method in operating upon 209 patients, with only 2 deaths. On the other hand, Harrington[10] has operated on 146 patients with pharyngoesophageal diverticulum by the one-stage technic, with no deaths and no complications; mediastinitis did not occur. Sweet[11] also reports a favorable experience in 5 cases and describes his technic of the one-stage operation. My own limited experience with the one-stage procedure has been similar. As Lahey[9] states "The decision to remove a pulsion diverticulum by one or two stages must be largely a matter of personal choice; the mortality of reported series done by both methods is approximately the same." Since the one-stage procedure entails fewer days of hospitalization — a matter of some consideration in the present economic era — it will be done with increasing frequency.

Diverticula of the thoracic esophagus are relatively uncommon, and the literature contains few contributions dealing with their treatment by surgical means. Actually, with better roentgenologic technics, the lesion is being encountered with increasing frequency, although the majority of cases so discovered are asymptomatic.

Janes[12] finds diverticula of the thoracic esophagus of two types, traction and pulsion. The former results from fixation of a point on the outer wall of the esophagus to an inflammatory area in relation to it, most often a tuberculous lymph node. It is, characteristically, of a more or less conical shape. Since the pulsion form presumably results from herniation of the mucous membrane through the muscular wall, it is enclosed only by mucosa, submucosa and fibrous tissue.

Dysphagia is the outstanding symptom and undoubtedly reflects the progressive mechanical obstruction of the esophagus by the enlarging dependent sac. As Adams[13] points out, in the traction type the sac rarely hangs down in a dependent position in relation to the esophagus or is rarely large enough to angulate or obstruct the esophagus and cause the classic symptoms. Occasionally, a small sac may cause acute obstructive symptoms should it become distended by an impaction of suitable material. On one such occasion, I removed, endoscopically from a thoracic diverticulum, large quantities of orange pulp to relieve obstruction some days prior to operation for removal of the sac.

Although small diverticula discovered routinely need no treatment, those that are large and are causing symptoms should be offered operation while

the patient is still in good condition. Adams[13] and Janes[12] concur in this point of view, which is now generally held. In 3 patients operated on before the era of antibiotics, Adams describes the operation of diverticulopexy, which was devised to circumvent infection by suspending the apex of the sac to the adjacent parietes to give it dependent drainage and relieve obstruction without opening the esophagus and courting the hazard of mediastinitis. Since the advent of penicillin and streptomycin, the direct attack by a transpleural operation, with the removal of the diverticulum in one stage similar to the technic used for the cervical variety, has proved to be a safe and satisfactory operation. In the reported cases[12-14] there have been no deaths. The operation has been carried out without incident in our clinics.

Cardiospasm

Cardiospasm or achalasia (absence of relaxation) has been recognized as a clinical entity for nearly three hundred years, and yet its etiology still remains unknown. Hypertrophy of the muscle in the region of the cardia has been the object of particular attention, but disintegration of the ganglions and connecting nerves of Auerbach's plexus has also been suggested as a factor in the production of the malady. The question of which is the primary cause is still unsettled since other observers[15] believe the degeneration of Auerbach's plexus to be secondary to the dilatation of the esophagus and not the cause of the cardiospasm. Whatever the etiology, the disease is a relatively common and distressing one and is therefore a matter of particular concern to the thoracic surgeon.

In a recent comprehensive review of the subject Wooler[15] discusses 47 cases that he studied. The disease occurs twice as commonly in women as in men and most often in the third decade. The high-strung, nervous person is more likely to be affected.

Cardiospasm affects the whole of the lower segment of the esophagus. It runs a continuous, slow, progressive course, which Wooler divides into two stages. The first is one of greatly increased activity of the esophagus during which the patient is "esophagus conscious" and may feel the esophagus go into spasm when he is excited. Anything other than the daily routine may bring on an attack. Food tends to regurgitate into the pharynx if the patient eats rapidly and, although the symptoms may vary from day to day, on the whole, they gradually worsen as the disease progresses. The stage of activity lasts for months until the esophagus tires of its increased effort and becomes passively dilated, ushering in the second stage, when most patients present themselves for treatment. The esophagus may be normal when symptoms of achalasia of the cardia are present, but such a normal esophagus may enlarge as the achalasia progresses.[16]

During the second stage, dysphagia and substernal discomfort increase in severity. In spite of increasing selectivity of diet, together with attempts to wash down food with fluids, the patient loses weight rapidly because he cannot take in sufficient food. Regurgitation of food into the mouth may occur at night when there is incompetence of the cricopharyngeus. Fluoroscopic examination of the esophagus with a barium swallow reveals great activity as in the first stage, but the waves of contraction fade out before they reach the constriction. Proximal to the constriction the esophagus appears to be immobile and dilated. After some years, all movements of the esophagus cease, and it becomes a large, patulous, tortuous bag.

In every case of cardiospasm, esophagoscopic examination should be made to rule out carcinoma before dilatations are undertaken. If the constriction at the cardia is due to cancer arising in the cardia of the stomach and infiltrating the walls of the esophagus, there may be no break in the mucosa although the type of resistance to the progress of the esophagoscope may arouse the suspicions of the operator. Under such circumstances, if no biopsy can be obtained, exploratory thoracotomy with actual inspection of the stenotic area is indicated.

Although the roentgenologic appearance of cardiospasm is quite characteristic, it should be recalled that other lesions of the lower esophagus causing dysphagia may be confused with it. These include benign strictures, possibly the result of peptic ulceration and frequently associated with hiatus hernia of the "short-esophagus" type (described below). In addition, lye strictures occurring commonly 5 to 8 cm. above the diaphragm may have to be considered in the differential diagnosis. Finally, the possibility of carcinoma of the esophagus in a long-standing case of cardiospasm cannot be ignored. I have seen such a coincidence in a patient known to have had cardiospasm for twenty years.

Most patients with cardiospasm can be cured by hydrostatic dilatations with the Plummer, Vinson, Moersch or Negus technic.[15, 17, 18] Thus Wooler[15] found 33 of 38 of his cases treated with the Negus dilator to be cured or improved. Clagett et al.[18] state that 70 per cent of their patients obtained complete relief after one treatment with the hydrostatic dilator.

A very small group, probably 2 to 5 per cent, of patients[18] will not obtain relief from dilatation, and in these cases surgical intervention is recommended. The choice of the type of operative procedure and the approach used will depend upon the individual operator.

Heller's operation, an extramucosal esophagocardiomyotomy similar to the Ramstedt operation for hypertrophic pyloric stenosis of children, performed through the chest, is advocated by Wooler.[15] Maingot[19] has cured 38 of 39 patients by this procedure. Some type of esophagogastrostomy is preferred by most surgeons. However, the fact that distressing symptoms of esophagitis due to reflux of

gastric secretions into the lower esophagus, although the obstruction to swallowing has been corrected, should be borne in mind. Clagett et al[18] prefer an esophagogastrostomy of the Finney pyloroplasty type performed transabdominally. Savinykh[20] reports 24 cases in which he performed esophagogastrostomy of the Heineke-Mikulicz type, using the abdominal approach. There were 2 deaths, but in the remaining 22 cases the results of the operation were good.

Kay[21] performed transpleural esophagogastrostomy on 17 patients. Postoperatively, there was symptomatic improvement and a pronounced reduction in the size of the esophagus. The Heineke-Mikulicz technic was used because it was thought to be easier than the Finney-type procedure. Nagel and Menke[17] have also operated transpleurally on 3 patients, performing gastrostomy of the Heineke–Mikulicz type.

On the infrequent occasions when the surgical treatment of cardiospasm has been considered necessary on the thoracic-surgery services at the Boston City and Massachusetts Memorial Hospitals, the transthoracic approach has been preferred because of its ease and flexibility in the event that any unexpected pathologic situations are encountered. The Finney pyloroplasty type of operation has been employed with satisfactory results and no mortality.

Strictures

Of recent years, interest has been directed toward the etiology of benign stricture of the lower esophagus. Although it may occur at any age, it is most often seen in people of middle age and has frequently been mistaken for carcinoma.

The condition has been imperfectly understood although often recognized to be associated with paraesophageal diaphragmatic hernia and, as a corollary, with the so-called congenitally short esophagus. In a careful study of 74 cases of peptic ulcer of the esophagus, Allison[22] has done much to clarify the situation in describing the sequence of events that leads to stricture as an end result. He believes that esophageal ulceration is almost always due to a diaphragmatic defect that permits herniation of the cardiac end of the stomach into the thorax. Since the prevention of regurgitation of gastric contents into the esophagus depends upon the "physiologic sphincter" at the cardia, and since this "sphincter" is competent only when the normal angle between cardia and esophagus exists, herniation, by distorting this relation, inevitably destroys the mechanism that prevents regurgitation. The resulting pathologic sequence is esophagitis, ulceration, fibrosis and stricture. Short esophagus is nearly always acquired in this way, even shortly after birth, and is rarely congenital. In cases of paraesophageal hernia, a concomitant hernia of the cardia, with ulceration, may be overlooked. In all cases the cardia should be exactly localized and esophagoscopy performed. In Allison's cases, conservative treatment and temporary jejunostomy were sometimes advised, but in 7 cases the stomach was replaced beneath the diaphragm and the diaphragmatic defect repaired. However, the esophagus must be elastic to permit this maneuver. In 5 cases, in which the esophagus was ulcerated and badly stenosed, the involved segment was resected, the upper end was anastomosed to a jejunal loop, and the stomach was excluded.

Olsen and Harrington[23, 24] are, for the main part, in agreement with Allison. To the etiologic factors in the production of short esophagus, they add reflex spasm of the lower part of the esophagus, which, they believe, results from stimulation of the vagus nerve and may be produced by a variety of digestive disorders. In their experience, dysphagia is the commonest symptom associated with short esophagus and, in the early stages, spasm may be the cause of the dysphagia; however, organic stenosis of the lower esophagus develops in most cases. They recommend that dilatations be used for the treatment of the dysphagia in the nonoperative cases. This should always be done over a previously swallowed string and never by blind bougienage.

In the opinion of Wangensteen[25] the esophagus is more susceptible than the stomach or duodenum to injury by the acid-peptic digestive juices, and the so-called idiopathic esophagitis and stricture are a manifestation of ulcer disease. He has observed 6 patients in whom extensive gastric resection did away with the necessity for continued dilatation of an esophageal stricture. He is also considering the idea of exploring the possibility of whether the dysphagia of cardiospasm, as well as that of bona fide lye stricture (of the lower esophagus), will respond to gastric resection, on the thesis that an active acid-peptic secretion may continue an established vicious circle.

The continuing surgical attack upon esophageal strictures of caustic or other origin, which have not yielded to bougienage, has been productive of ingenious technics for the construction of an artificial esophagus or re-establishment of continuity between mouth and stomach.

Gross[26] has demonstrated the practicality of resecting a 3-cm. segment of an infant's esophagus for a short stricture and performing end-to-end anastomosis. The recovery was uneventful, and the deglutition, seven weeks later, excellent. Tuttle and Day[27] have similarly treated 6 patients with short strictures by complete or wedging types of resections, with good functional results in each case.

When stricture involves a great portion or the entire length of the esophagus, the problem requires the transplantation of small bowel, or stomach, to re-establish continuity. Yudin[28] has summarized the technics up to 1944 and has reported his remarkable experience with 80 cases. Longmire[29] has described a procedure for the construction of an

antethoracic esophagus by using transplanted jejunum within a skin tube and the preservation of its blood supply by anastomosis to the internal mammary vessels.

The antethoracic esophagus, to circumvent strictures, whether it is formed by the transplanted jejunum or by the skin tube, is difficult to construct and has recognized disadvantages. Certainly, it is preferable for continuity between mouth and stomach to be established along its normal route within the thorax. To this end, Rienhoff[30] has successfully transplanted the jejunum intrathoracically in 3 cases after resection of the esophagus. He believes that from the standpoint of length available and the size of the eventual tube, the jejunum is better suited to take the place of the esophagus in the mediastinum than the bulky stomach pulled up to perform the same function. Harrison[31] has also reported 2 cases in which complete lye strictures of the cervical esophagus were treated by transthoracic substitution of a loop of jejunum for the esophagus. He performed the operation in three stages. The first stage, performed through the abdomen, entails the isolation of a segment of jejunum whose blood supply will have adequate length to reach the neck without undue tension and without too much redundancy of bowel, and at the same time, the distal end of the jejunal loop is anastomosed to the stomach. In the second stage, performed through the left pleura, the isolated segment of jejunum is brought up into the neck, being made to lie in the bed of the resected esophagus, and, at a subsequent stage, when the mediastinum is well sealed, the anastomosis between esophagus and jejunum is made in the neck without fear of possible leakage.

Sweet[32] has reported a successful experience with intrathoracic esophagogastrostomy with high anastomosis for strictures not involving the cervical segment. I have had a similar experience in 3 cases. In cases of congenital atresia with tracheoesophageal fistula in which primary anastomosis is impossible because of the length of the atretic segment, Sweet[33] has restored continuity of the alimentary tract by performing intracervical esophagogastric anastomosis after the stomach is pulled up through the chest.

Following upon the remarkable accomplishments of recent surgery in its successes achieved in the treatment of carcinoma of the esophagus, these technics offer much to patients afflicted with benign strictures, heretofore doomed to the circumscribed life attendant upon gastrostomy or perpetual bougienage.

Esophageal Varices

Esophageal varices are local manifestations of portal hypertension. However, when hemorrhage occurs from them, the situation frequently takes on the aspects of an emergency, and efforts to arrest the bleeding must be directed toward the varices themselves. Moreover, as Carter and Zamcheck[34] point out, the prompt diagnosis of the cause of bleeding in patients with massive hemorrhage from the upper esophagogastrointestinal tract is difficult, and patients bleeding from esophageal varices must be distinguished from those bleeding from other lesions inasmuch as prognosis, as well as therapy, depends upon the cause of bleeding and a decision for emergency operation requires early diagnosis. These authors demonstrate the value of esophagoscopy in a series of such cases at the Boston City Hospital. The use of Oxycel gauze tampons passed through the esophagoscope as a definitive hemostatic measure was shown to be of value, and has since been used repeatedly, with success, in arresting this type of bleeding.

Bleeding from this source has also been effectually controlled by tamponage, an inflatable latex bag inserted into the esophagus[35] being used.

Obviously, these are palliative and temporary measures, and if recurrences are to be prevented, definitive operative intervention by means of one of the shunt operations must be undertaken. When bleeding has been massive and frequently intermittent, despite temporary arrest by Oxycel tamponage, Ware[36] has opened the left pleural cavity and ligated all the visible venous connections to the esophagus above and below the diaphragm. This resulted in cessation of bleeding so that ten days later splenorenal venous shunt could be undertaken successfully.

Som and Garlock[37] have packed with gauze the posterior mediastinum about the esophagus above the level of the aortic arch, in a man with esophageal bleeding whose condition had become desperate. Esophagoscopy four months later showed the upper three fourths of the esophagus to consist of normal and shrunken fibrotic varices around the cardia. The idea is based on the supposition that establishment of a large area of granulation tissue external to the muscular layer of the esophagus at a distance removed from the seat of the varices will result in a collateral circulation that will be outside the esophagus, thereby taking the load off the venous pressure in the esophageal varices, which lie in the vulnerable submucosal position.

We have used this operation in an elderly cirrhotic patient whose liver function and general condition were such as to preclude more radical procedures. She had one episode of bleeding about a month after operation but has had none in the succeeding seven months. The rationale of the operation is still open to speculation.

Although it is not within the province of this report to enter upon a discussion of portal hypertension, so far as it touches upon hemorrhage from esophageal varices, one should give reference to the ideas of Wangensteen's group as discussed by Baronofsky.[38] Their thesis is that the regurgitation

of gastric secretions into the lower esophagus is poorly tolerated by the impaired esophageal mucosa, with consequent ulceration and bleeding from the underlying varices. They propose, on the basis of experimental work, that the acid-peptic factor may be considered as important in the bleeding of esophageal varices as the hydrostatic factor and that one must therefore do something akin to total gastrectomy to afford absolute protection. Their reported 8 cases are, for various reasons, far from conclusive.

Phemister and Humphreys[39] have performed total gastrectomy and esophagogastric resection for the bleeding due to Banti's syndrome.

However, as Baronofsky[38] indicates, all operative procedures directed at correcting hemorrhage in hepatic cirrhosis are essentially palliative in nature, for there is no known means of arresting cirrhosis itself. Yet life may be prolonged through operative procedures that lessen the tendency to hemorrhage.

Further clarification of this aspect of the problem must wait upon a broader knowledge, more cases and a longer follow-up period.

Benign Tumors

Although benign tumors of the esophagus are relatively infrequent, this does militate against the importance of diagnosis and treatment when they do occur. The treatment of these potentially malignant lesions is of particular interest to the thoracic surgeon because operative procedures of some magnitude may be necessary to effect their removal.

A wide variety of histopathological types has been described in the literature[40]; those encountered most frequently have been myomas, leiomyomas, fibromas and polyps. Harrington and Moersch[41] divide these benign tumors into two main groups: the mucosal and the extramucosal. The former usually are fibrolipomas or fibromyxomas and are covered by normal epithelium of the esophagus. They are often pedunculated and arise from the submucosa. The extramucosal or intramural tumors arise from the muscle of the wall of the esophagus; they do not involve the mucosa and usually are leiomyomas.

These benign tumors grow slowly and may reach a considerable size before causing symptoms. Those located intramurally tend not to produce obstruction of the esophagus until they attain great bulk. The symptoms, as might be expected, are dysphagia, substernal pain, regurgitation of food, cough and dyspnea.

Barrett[42] has described a huge fibroma of the esophagus, the patient having been admitted as a case of bronchial obstruction. There were no symptoms referable to the esophagus, and yet at operation it would have been necessary to resect a great part of the esophagus to effect a cure.

The pedunculated tumors frequently give rise to obstructive symptoms, and their diagnosis is often made apparent by regurgitation of the tumor into the mouth, which may be the first subjective symptom.[40, 41] Such a tumor may be fraught with hazard to life inasmuch as regurgitation into the nasopharynx may block the trachea and result in strangulation.

The diagnosis can usually be arrived at by roentgenographic and roentgenoscopic examination, together with esophagoscopy. By the latter means the exact site of origin of the pedunculated tumors can, as a rule, be determined.

The surgical treatment of these tumors depends on whether the growth is submucous or pedunculated, or on whether it arises from the outer portion of the muscular coat of the esophagus. Pedunculated tumors that are small and have their origin high at the introitus may be removed through the mouth with a snare and cautery.[41, 43] Larger tumors of this type require cervical esophagotomy. If they are huge, or if the pedicle is situated low in the esophagus, they may require transpleural esophagotomy.

If only a segment of the wall is involved, the intramural tumors may be removed by local excision with subsequent reconstruction of the esophagus. However, if the tumor involves the entire wall, partial resection of the esophagus, with esophagogastrostomy, may be the technical procedure of choice.

Carcinoma of the Esophagus

As has always been true in the surgical attack upon any lesion of any organ, once the feasibility of the fundamental procedure has been demonstrated, the technics assume increasing importance. This has become evident in recent years in the developmental phases of the treatment of carcinoma of the esophagus since transthoracic resection with intrathoracic esophagogastrostomy was first shown to be the method of choice by Adams and Phemister.[44] It has been directed principally toward widening the indications in the difficult problems that are presented particularly when carcinoma occurs, fortunately infrequently, in the upper fourth, between the top of the arch of the aorta and the end of the cervical esophagus. Stated otherwise, it has been concerned with the technical problems involved in bridging the wide gap that remains when the tumor is resected from high thoracic and low cervical esophageal levels.

Some aspects of carcinoma of the high thoracic and cervical portions of the esophagus are such as to render its consideration apart from similar lesions occurring in the lower three fourths. Although Wookey's[45] operation has been eminently successful in extirpating cervical esophageal lesions and in restoring continuity, the cure rate has been discouraging because of the high rate of recurrence in

the regional cervical lymph nodes, to which cancers at this level are prone to metastasize. As Bricker et al.[46] point out, rational cancer surgery unequivocally demands the removal of the entire node-bearing area of the involved structure and the radical extirpation of the lesion. The requirements of a satisfactory cancer resection are well fulfilled for carcinoma at and below the level of the aortic arch by the procedure of resection and esophgogastrostomy in one stage. It seems that combined cervicothoracic resection, with radical resection of the regional nodes bilaterally en bloc, would more nearly satisfy the requirements of an ideal cancer resection in carcinoma of the upper esophagus. With these criteria in mind Bricker and his associates have devised and carried out such an operation on one patient, although because of technical difficulties, a satisfactory neck dissection was not included. Briefly, the operation, which was performed in multiple stages, entailed mobilization of the tumor through a right anterior thoracotomy with division and closure of the distal esophagus. The proximal portion of the esophagus with the tumor-bearing area was brought through a left cervical incision, and after amputation, the normal proximal portion of the esophagus was fixed to the skin. During subsequent stages a pedicled tube was raised from the skin of the anterior wall of the chest, brought through the old cervical incision into the right pleura via the superior thoracic aperture and anastomosed to the remaining distal end of the esophagus, re-establishing continuity from pharynx to stomach.

Although this is a laborious and multistaged procedure, it deserves further trial and may prove to be a valuable addition to the surgical armamentarium for the treatment of esophageal cancer at high levels.

Cancers occurring in the upper fourth of the thoracic esophagus have, until recently, presented insuperable problems. Too low for the Wookey operation, they are, for the most part, too high to be adapted to an intrathoracic esophagogastrostomy. Recently, Sweet[47] has successfully circumvented this difficulty by bringing the stomach, after mobilization, into the neck through the left side of the thorax and performing cervical esophagogastrostomy through a separate incision in the neck. To facilitate his exposure for the performance of the anastomosis and to avoid possible compression, he resected the inner half of the left clavicle and a corresponding segment of the first rib. Previously, Garlock[48] had made a similar attempt, which, although technically successful, had ended fatally for reasons not entirely clear. With subsequent reports[49-52] of successful cases handled by modifications of this technic, the procedure has proved to be an important contribution to the surgical treatment of lesions at this level.

For cancers occurring below the level of the aortic arch down to and in the gastric cardia, transthoracic resection and intrathoracic esophagogastrostomy continue to be the mandatory procedure, offering the greatest chance of cure and the longest period of survival with worthwhile palliation. In this group, when the cancer exists in the midthoracic esophagus necessitating supra-aortic anastomosis, the operative mortality has been considerably higher than when the location of the tumor is such that anastomosis can be made below the aortic arch. The desirability of reporting these procedures separately has been pointed out by Strieder[53] inasmuch as some cancers occurring in the lower portion of the midthoracic zone may be amenable to infra-aortic anastomosis. Thus, Sweet[54] reports a mortality of 12 per cent in 109 cases of low resection, and a mortality of 24.1 per cent in 29 patients who had supra-aortic anastomosis. The experience of Strieder and Lynch[55] since 1945 parallels this, with a mortality of 17.2 per cent in 58 low resections but one of 30.7 per cent in 26 resections with supra-aortic anastomosis.

The resectability rate of carcinoma of the esophagus has increased with improvement in the technic although the definition of resectability needs clarification. In a previous progress report, Scannell[56] found that of 589 collected cases, 343, or 58 per cent, were resected. In the series referred to above,[55] the rate is slightly higher, 67 per cent of 145 cases since 1941, but it must be understood that many of these resections were performed only with the hope of palliation and without hope of cure.

I have taken the attitude that no patient should be denied the opportunity for resection and palliation until he has been explored, unless it is obvious that his general condition is so desperate that he cannot withstand operation or that after trial he cannot be improved by general measures to a point where operation is feasible. Such a philosophy has frequently entailed leaving gross tumor behind in cases that were not in a strict technical sense operable. As such, they have not been cancer operations but palliative ones, and yet the results are considered to have justified a continuance of this policy. The only alternatives are radiation therapy and dilatation or gastrostomy, or both.

Cooper and Buxton[57] have recently analyzed 194 cases in which gastrostomy was done during a thirteen-year period at the University of Michigan Hospital in order to evaluate the procedure as a palliative and a therapeutic measure. In the series 144 patients had malignant lesions (109 of the esophagus, 22 of the gastric cardia, 11 of the larynx, and 2 of the bronchus) for which gastrostomy was performed; of the 194 patients, only 18 were alive at the time of the report. Seventeen of these 18 had non-neoplastic, presumably curable, disease. From the data, the authors conclude that palliative gastrostomy in a patient with inoperable malignant

neoplasm or other hopelessly incurable lesion produces no significant extension of life and no demonstrable nutritional improvement. This appears to reflect the opinion of most surgeons who cope with these problems. Certainly, it is my opinion, and is the one by which our Thoracic Surgery Services are guided.

With the risk of establishment of esophagogastric continuity by a transthoracic operation comparable to that of gastrostomy in a similar patient and with at least equal, if not greater survival time, during which the patient is able to swallow, there appears to be ample justification for the definitive operation as a palliative measure.

In the unhappy event that the lesion is completely inoperable because of fixation and infiltration of surrounding vital structures, Allison[58] has proposed, and carried out in 2 cases, by-passing the growth by performing esophagojejunostomy proximal to the tumor after the manner of the Roux "Y" technic. Both patients survived for six months and could swallow normally to the end.

Under certain circumstances there will arise the question of reoperation upon patients who have been previously subjected to transthoracic resection of cancers of the esophagus or gastric cardia, and who return with early evidence of recurrence at the site of anastomosis. In view of the well known propensity of cancer in these locations to extend submucosally for long distances up the esophagus, it now appears to be an essential part of the routine at operation to have frozen-section examination of the divided end of the resected esophagus. If, at the time of the original operation, there has been no evidence of extension of the primary growth beyond its local confines, serious consideration should be given to reoperation upon such a patient who is otherwise a suitable candidate.

Under these conditions, the first successful reoperation upon a patient with evidence of recurrence at the site of anastomosis was reported by Strieder.[53] At the time of this report the patient is alive, well and swallowing almost normally, four years and two months later. Since that time, Pack and McNeer[59] have reported a similar operative survival in which recurrence became apparent one month after transthoracic total gastrectomy with esophagojejunostomy for cancer of the gastric cardia. Recently, Smithwick[60] has also described a survival after transthoracic resection of recurrent carcinoma of the lower fourth of the esophagus. At the original operation, an extremely short jejunal mesentery was noted, and because this precluded an esophagojejunostomy at the time of the second procedure, the transverse colon was used for an esophagocolostomy. Previously, preliminary gastrostomy had been made for the obstruction, and a right transverse colostomy was done to facilitate preparation of the bowel. At a subsequent stage the continuity of the esophagogastrointestinal tract was re-established, leaving a transplanted segment of the colon within the left pleural cavity. It is of considerably more than passing interest, in the cases in which the transplanted segment is left in the pleural cavity, that by a careful plan of bacteriologic study and the appropriate selection of antibacterial agents, Howe[61] was able completely to sterilize the defunctionalized loop of transverse colon in preparation for its anastomosis with the esophagus. These 3 cases demonstrate the feasibility of operation for recurrent cancer if there is no evidence of distant metastases.

The resection of a segment of the esophagus for tumor or stricture followed by primary end-to-end anastomosis has, hitherto, been fraught with considerable hazard and has not been considered a safe or feasible procedure. The difficulties have stemmed partly from an imperfect understanding of the blood supply of the esophagus, the paucity of which has been considered responsible for poor healing and disruption of the anastomosis with all the fatal sequelae. Other factors, however, such as trauma during handling and failure to make a meticulous anastomosis have contributed to the recorded failures. The possible etiologic role of ischemic necrosis in early diastasis and leakage or, in delayed obliterative fibrosis and stricture, of reconstructive esophageal anastomotic suture lines at various levels is considered by Shapiro and Robillard[62] in a recent survey of the arterial supply of the esophagus. As a result of their dissections of 50 bodies, they conclude that the esophageal circulation is best considered as a *shared* vasculature, and that due care must be taken during surgical mobilization in separating the esophagus from such embryologically related structures as the trachea, bronchi and diaphragm, lest the freed segments be devascularized to a degree incompatible with reparative processes. Reference has already been made to the reports of Gross[26] and Tuttle and Day[27] concerning the successful resection of short strictures with the immediate performance of end-to-end esophageal reconstruction.

Because of the tendency of esophageal cancer to progress in the wall of the organ both by invasion and by lymphatic extension, the usefulness of short resections with end-to-end anastomosis is extremely limited for this lesion. However, by this technic Strieder and Lynch[55] resected a 6-cm. segment for a very small, well localized cancer at the level of the aortic arch in a forty-year-old man who had had extensive gastric surgery for ulcer some years previously. Because the technical procedures below the diaphragm, which were necessary before continuity of the esophagogastrointestinal tract could be re-established, added up to a formidable operation, and because there was no evidence of extension beyond the esophagus, a local resection was carried out. Examination of the specimen revealed that the tumor was completely removed. The pa-

tient had an uneventful recovery and was well, without evidence of recurrence, over a year later.

It is conceivable that the procedure might be indicated for palliation alone, or in an elderly patient with a small tumor whose condition warrants termination of the operation in the simplest way at the earliest moment.

Radiation therapy undoubtedly has its place in the treatment of carcinoma of the esophagus. In my experience it should be reserved for cases in which exploration reveals fixation and direct extension to contiguous structures, principally the aorta, to a degree that no palliative operation can be offered with reasonable promise of success. In occasional cases there has been a remarkable response to radiotherapy in terms of palliation and prolongation of life.

Recently, Brown[63] inserted an 8-mm. silver tube into the lumen of an inoperable esophageal cancer and fixed it in position. The patient could be fed by mouth at once and was immediately treated by roentgen-ray radiation according to the multiple-port method of Demy over a period of thirty-one days. This caused rapid recession of the mass, and the tube passed spontaneously in thirty days. Esophagoscopy six months after radiation revealed a patent lumen and no evidence of cancer.

In Copenhagen, only the occasional case comes to surgery because here Nielsen has been an enthusiastic advocate of his "rotation-radiation" technic. By this means, the patient, seated in a special stool, is rotated with the esophagus as his long axis, at right angles to the field of radiation, so that the maximal dosage is delivered to the tumor, with minimal skin effect.

As Scannell[56] points out, however, only 25 per cent of the patients in Nielsen's series were alive at one year, and 15 per cent at two years; whereas, in Sweet's resected cases, 42 per cent of the patients were alive at one year and 34 per cent survived for two years.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

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CASE 36381

PRESENTATION OF CASE

A sixty-nine-year-old woman was admitted to the hospital with the chief complaint of malnutrition.

The patient had been in good health until about four months prior to admission, when she first noticed a dry, hacking cough, productive of a little whitish phlegm, that became more pronounced. There was no dyspnea, wheezing, hoarseness, purulent expectoration or hemoptysis. Two months prior to admission while at work she had a severe spell of coughing, following which she was too weak to continue work and did not return to it again. The patient was sent to a rest home for two weeks, without improvement, and from there was admitted to another hospital. At that time she noted occasional night sweats and was told she ran a high temperature, but had no chills. X-ray films showed emphysematous changes in the lungs, calcified uterine fibroids, and hypertrophic arthritis. A cholecystogram showed a nonfunctioning gall bladder with calculi, and a gastrointestinal series and barium-enema examination were negative. Although the cough decreased on treatment with Crysticillin and streptomycin, the fever persisted, and the patient was referred to this hospital for further study. Her weight, which had customarily been 95 pounds had decreased to 67 pounds at the time of admission. There had been a transitory complaint of calf tenderness during the week after the patient ceased working, but this complaint had disappeared by the time of admission.

The family history was noncontributory. The patient had known of high blood pressure of an unspecified amount for about six months. She had always been constipated, and there was no change in bowel habits. She had undergone a normal menopause many years previously.

Physical examination showed a pale, markedly cachectic woman who coughed occasionally. There was decreased hearing in both ears, slight internal strabismus of the left eye, Grade I arteriosclerotic changes of the fundi, edentia, a red and furry tongue without atrophy, slight distention of the neck veins when she was sitting, and a few shotty inguinal lymph nodes. There was a slight increase in the anteroposterior diameter of the chest, with coarse rales posteriorly on the left at the tracheal bifurcation, and limited motions of both leaves of the diaphragm. The liver edge was palpated two fingerbreadths below the costal margin. There was absent vibratory sense in the lower extremities; all other senses were intact. The reflexes were equal and active, although there was generalized muscular wasting and poor strength. Examination of the heart showed the aortic second sound to be equal to the pulmonic second sound. There were no significant murmurs, and the sounds were of good quality. There was no clubbing or ankle edema. Pulses in the extremities were good.

The temperature was 99.6°F., the pulse 120, and the respirations 25. The blood pressure was 190 systolic, 90 diastolic.

Examination of the blood showed a white-cell count of 24,400, with 81 per cent neutrophils, 11 per cent stab forms, 4 per cent lymphocytes, 2 per cent monocytes and 2 per cent eosinophils. The hemoglobin was 7.5 gm., the hematocrit 32 per cent, and the red-cell count 3,400,000. The cells showed a moderate hypochromia with a mean corpuscular volume (MCV) of 93 cubic microns and mean corpuscular hemoglobin concentration (MCHC) of 26 per cent. The urine was clear yellow, with a specific gravity of 1.020, gave a + test for albumin and contained no sugar; the sediment contained 2 to 5 white blood cells per high-power field, no red blood cells and frequent granular and hyaline casts. The nonprotein nitrogen was 30 mg., the

albumin 3.88 gm., and the globulin 2.37 gm. per 100 cc. (albumin-globulin ratio of 1.2). The cephalin-flocculation and bromsulfalein tests were negative. Repeated stool specimens were guaiac negative. X-ray examination of the chest showed low leaves of the diaphragm, increase in the anteroposterior diameter and multiple areas of patchy haziness and linear density throughout both lung fields, most marked on the left anteriorly in the region of the lingula, where there were apparently dilated bronchi. No definite intrabronchial lesions or metastases were seen. The liver and spleen were not enlarged. The kidneys were not well seen. A 1-cm. gallstone and a large calcified mass in the pelvis consistent with calcified fibroids were identified. The bones were somewhat osteoporotic. The aorta was moderately tortuous, and calcifications were noted in the walls of the pelvic arteries.

On the second hospital day and thereafter a friction rub was noted in the left axilla, fairly high up and Grade III in intensity. The temperature remained elevated, with a daily afternoon spike to about 102°F., for the first two weeks in the hospital. An attempt was made to give a high-calorie diet, but the intake averaged between 1500 and 1600 calories per day, with 1900 calories the highest on any single day. A barium-enema examination was negative. Repeat chest films with fluoroscopy showed no change in the intervening three days. Metastatic series showed no recognizable bone metastases. At this time a chest-survey report arrived stating that the film taken a month prior to admission had shown clear lung fields. Of four sputum examinations for tumor cells one was negative, and three were unsatisfactory. Urine cultures showed beta-hemolytic streptococci and a moderate growth of *Staphylococcus albus*. After two weeks in the hospital repeat chest films showed little change, and the patient's condition remained the same. It was therefore thought advisable to start chemotherapy. Thirty-one grams of aureomycin was given over a period of ten days, with a satisfactory temperature response and some diminution of the densities noted on the chest x-ray films but with the appearance of fluid in the left pleural space. The white-cell count, however, remained at around 24,000. The patient felt somewhat improved subjectively at that time. The urinary sediment showed a few white cells and occasional red cells, with granular casts, and there was a ++ test for albumin. Cultures of the urine during this period showed no growth. The blood cultures showed no growth. Tularemia, brucella and Weil–Felix agglutinations were negative. A survey of the blood chemical constituents on the thirteenth day revealed a serum calcium of 6.6 mg., phosphorus of 6.2 mg. and phosphatase of 4.4 units per 100 cc. Repeat determinations showed a calcium of 8.2 mg., phosphorus of 8.3 mg. and alkaline phosphatase of 9.4 units per 100 cc. In view of the abnormal blood chemical findings an excretory urogram was performed, which showed no excretion of contrast material up to forty-five minutes. On the twenty-third hospital day the nonprotein nitrogen was 250 mg., the uric acid 8.0 mg., and the creatinine 6.8 mg. per 100 cc., and the carbon dioxide 13.7 milliequiv., the sodium 137.4 milliequiv., the potassium 7.3 milliequiv., and the chloride 97 milliequiv. per liter.

At about this time there was an onset of paralysis of the right peroneal nerve, without other demonstrable physical findings in the right leg. The dorsalis-pedis pulse was palpable. There was no swelling or tenderness of the leg, no Homans sign, no meningeal signs and no headache or stiff neck. The friction rub in the left axilla had been gradually lessening but was still present. The dietary intake began to fall off markedly, and supplementation with intravenous administration of fluids and blood transfusion was begun. Sodium lactate was added to the fluids. Three days later the nonprotein nitrogen was 210 mg. per 100 cc., and the carbon dioxide 10 milliequiv., and the potassium 6.8 milliequiv. per liter. In spite of the moderate chemical improvement the patient became disoriented, and a friction rub appeared at the apex of the heart.

On the following day she became more confused and progressively more dyspneic; the pulse was 110, the respirations 30, and the blood pressure down to 120 systolic, 80 diastolic. Coarse rales and squeaks appeared throughout the chest. The nonprotein nitrogen was 220 mg. per 100 cc., and the carbon dioxide 14 milliequiv. per liter.

It was planned to dialyze the patient with the artificial kidney, but she died on the twenty-eighth hospital day before this procedure was carried out.

Differential Diagnosis

Dr. Jacob Lerman*: It seems that the problem here is to determine the nature of the pulmonary lesions and the cause of the uremia. Let us first dispose of the anemia. There are some clinical features that suggest pernicious anemia. The patient had a red tongue and a loss of vibratory sense. However, the anemia itself was not macrocytic or hyperchromic, and there was not an abnormal number of macrocytes in the smear. Thus, in spite of the clinical suggestions we shall have to discard the possibility of pernicious anemia.

The x-ray findings in this hospital were different from those taken outside a month or so previously. May we see the x-ray films now?

Dr. Stanley M. Wyman: The film Dr. Lerman referred to as showing findings different from ours was taken during a chest survey. I think the report probably means that the examination was considered negative for tuberculosis. We have one film taken in the other hospital a week before admission that I shall not show, since it was essentially the same as those taken here. The films of the chest show the

*Associate physician, Massachusetts General Hospital.

diaphragm to be low and the lung fields bright — the chest being increased in anteroposterior diameter. There are multiple, linear and somewhat mottled densities in both lung fields consistent with long-standing disease, probably emphysema and fibrosis with old infarct scars. There may be some associated bronchiectasis. On the grid film the major bronchi are fairly well outlined, and there is no evidence of intrinsic disease in the bronchi. The film of the chest taken eleven days after the initial examination discloses a slight increase in the process in the left-lower-lung field that may be pneumonitis. The barium-enema study reveals no intrinsic disease. I think the liver does lie low in position, but there is no evident enlargement. The gallstone is well seen lying above the hepatic flexure of the colon, and there is a suggestion of indentation of that portion of the colon by extrinsic pressure. The last two films selected from the attempted intravenous pyelogram show no evidence of contrast substance excreted in forty-five minutes.

DR. LERMAN: Apparently, the Service considered pulmonary neoplasm very seriously and certainly made every effort to rule it out. Considering the intensive search as well as the absence of clubbed fingers, rapid development of physical signs and the changes in the x-ray appearance, it seems that cancer — either metastatic or primary — is unlikely. I think I shall just mention tuberculosis as a possibility. It was undoubtedly searched for, but there was very little evidence for it. Dr. Wyman mentioned chronic pulmonary fibrosis with bronchiectasis. In addition there was evidence of right-sided heart failure as indicated by pulmonary congestion and distended neck veins. There was terminal heart failure. One must consider repeated pulmonary infarcts as an explanation of the changes in the lungs. There was a history suggestive of thrombophlebitis. The x-ray changes, the history of calf tenderness and the improvement with aureomycin are consistent with a diagnosis of chronic pulmonary infarcts. Dr. Wyman, would you say that there is evidence of congestion in the areas adjacent to the mediastinum?

DR. WYMAN: The main hilar shadows are prominent, but the patient was lying on her back and it is very difficult for me to be certain how real the changes are.

DR. LERMAN: The physical signs mentioned above, the rales heard in the chest posteriorly and the suggestive x-ray findings certainly indicate that there was an element of pulmonary hypertension with right-sided heart failure in addition to any other lesion in the lungs.

The more difficult thing to explain is the cause of the renal failure. The first examination of the urine was not indicative of anything seriously wrong with the kidneys. There were a good many casts and a + test for albumin and a few white cells in the sediment. A positive culture obtained later verifies a diagnosis of pyelonephritis, which apparently improved with antibiotic therapy. The rapid development of phosphate retention, with low calcium in the blood, and marked retention of uric acid and creatinine suggest that renal failure had been going on to a slight degree for many months. The most likely cause of the failure is chronic pyelonephritis. Other possibilities that would have to be considered are chronic glomerulonephritis, which is difficult to exclude but for which there is not enough evidence, and nephrosclerosis as the result of long-standing hypertension and arteriosclerosis. For some reason I am intrigued with the possibility of amyloid disease of the kidney, mainly because the patient had long-standing cachexia and bronchiectasis. A slowly progressive amyloid disease of the kidney can end up in renal failure with a shrunken kidney in the same fashion as nephrosclerosis. One bit of evidence in favor of this diagnosis is the unusually large number of casts in the urine specimens, as compared with the small amount of albumin and the few white cells. There is no reason why this patient could not have had both chronic pyelonephritis and amyloid disease of the kidney. Perhaps chronic infection was conducive to the development of amyloid disease.

I wondered whether or not antibiotics could have contributed to the development of renal failure. Certainly, we have not heard of renal failure resulting from penicillin or streptomycin. She also received aureomycin, but I have not been able to find anything in the literature that suggests that aureomycin can produce damage to the kidneys in the same fashion that sulfonamides do. Consequently, I think I shall have to dismiss the treatment with antibiotics as a cause of renal failure.

I am left with an unsatisfactory explanation of all the findings. I can only surmise that this patient probably had chronic pyelonephritis and possibly amyloid disease of the kidney, multiple pulmonary emboli and bronchiectasis, uremic pericarditis and chronic congestive heart failure.

DR. ANDRIES QUERIDO: I think that a combination of a long-lasting fever, a progressive kidney disease ending up with kidney insufficiency, paralysis and lung lesions would make me consider the possibility of periarteritis nodosa.

DR. LERMAN: I did not mention anything about the nerve lesion because it seemed to me that the paralysis of the peroneal nerve was a "red herring." I could not tie it in with the other clinical findings and assumed it to be due to pressure.

DR. MYLES P. BAKER: The Service was much discomfited by the rather rapid development of kidney failure in this case. We had not expected it, as was obvious from the protocol. The picture of the lung lesion was obscure to us. It was a singularly dry bronchiectasis. I do not recall hearing rales. As noted, there was no purulent sputum. The patient presented a picture of fever of unknown origin,

not a septic-looking fever chart, but with an evening rise of temperature to 100 and 101°F., much like what one sees in persons with malignant neoplasm, and the search for the basis of the fever occupied most of the first week or ten days in the hospital. The opinion of the Radiology Department was that the lung lesion was consistent with bronchiectasis, and it was with that in mind that we resorted to the aureomycin therapy. I was struck by the fact that the white-cell count did not come down to more normal figures when the fever relented. The renal failure appeared a little sooner than one would make out from the protocol, about the time the aureomycin was started, and the patient rapidly failed in a few days. It was suggested by one of the members of the staff that the combination of fever of unknown origin, leukocytosis, the appearance of paralysis of the peroneal nerve and the rapid decline in uremia would be consistent with a diagnosis of periarteritis nodosa. We put a question mark in front of it but thought it might explain this rather unusual onset of renal insufficiency in a patient hitherto unsuspected of having such a condition.

Dr. Wyman: There is one thing I neglected to mention, and that is the bone picture, which is one of osteoporosis. Although we did not find frank localized disease I think one always has to think of widespread metastases in such a case. The second thing that intrigues me is the gallstone, which seems to have shifted considerably in position, and I wonder whether or not the gall bladder is large.

Dr. Baker: The patient had had one attack of abdominal pain prior to admission to the hospital.

Dr. Lerman: At one point I thought of the possibility of generalized lymphoma as an explanation for the fever, pulmonary lesions and osteoporosis, but I could not find anything in the description of the x-ray film to confirm this. I thought the x-ray films would make a diagnosis for us.

Dr. Helen S. Pittman: How about myeloma? Is not that one of the things that would fit with the changes in the chemical constituents later on and also could be accompanied by rapid renal failure?

Dr. Tracy B. Mallory: It is quite possible. Diffuse osteoporosis would be consistent with it.

Clinical Diagnoses

?Periarteritis nodosa.
Uremia.
Bronchiectasis.

Dr. Lerman's Diagnoses

Chronic pyelonephritis, with amyloidosis.
Uremic pericarditis.
Pulmonary emboli.
Bronchiectasis.

Anatomical Diagnoses

Wegener's granulomatosis involving lungs, kidneys and spleen.
Bronchiectasis, chronic, bilateral, moderate.
Pericarditis, serofibrinous (uremic).
Cholelithiasis.
Leiomyoma of uterus, calcified.
Atheromatosis of aorta, moderate.

Pathological Discussion

Dr. Mallory: The autopsy findings were very unusual, and we did not know what to make of them in gross. The lungs showed multiple foci of fibrosis in which were small areas of necrosis that were not frankly purulent or caseous. There was some degree of dilatation of the bronchi of the lower lobe, a mild bronchiectasis, but the fibrotic lesions appeared to be something separate. There was a fibrinous pericarditis, without much question uremic in origin. The kidneys were somewhat smaller than normal in weight and showed cortexes that were only half the normal thickness and were very dense, fibrotic and scarred. They were largely white, but there were irregular, red hemorrhagic areas, which slightly suggested infarction. The pyramids, in contrast, were normal in appearance. Nothing else of importance was noted at autopsy except the calcified fibroids, the gallstone and other factors already known about.

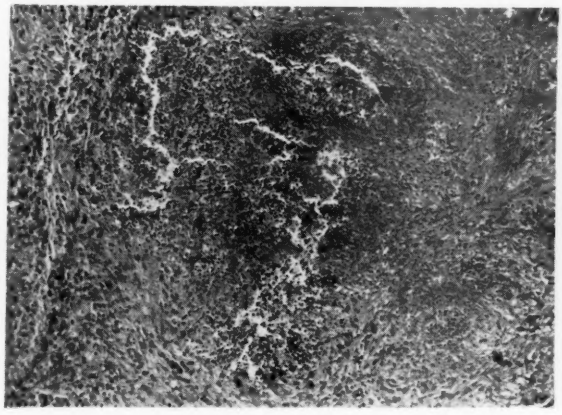

Figure 1.

The microscopical sections, which only came through yesterday afternoon and which I have been worrying about ever since, revealed extensive granulomatous lesions in the lungs and kidneys and two small foci in the spleen. In the lungs these lesions showed many irregular giant cells and numerous foci of necrosis, but nothing that even suggested a characteristic tubercle (Fig. 1). No organisms could be identified in spite of a very

careful search because of the possibility of histoplasmosis. In the kidney a few entirely similar granulomas were found, but the most striking lesion consisted of a series of vessel changes, of which some were endarterial, some periarterial and some associated with destruction of the arterial wall and aneurysm formation (Fig. 2). The picture suggested but was not entirely characteristic of a periarteritis nodosa. In searching for a possible way to tie these things together, I was reminded of a description presented in 1936 and 1939 by Wegener[1, 2] of a lesion of the respiratory tract, granulomatous in character, associated with arterial lesions, which he described as resembling very closely periarteritis nodosa and associated in all these cases with similar lesions in the kidney and

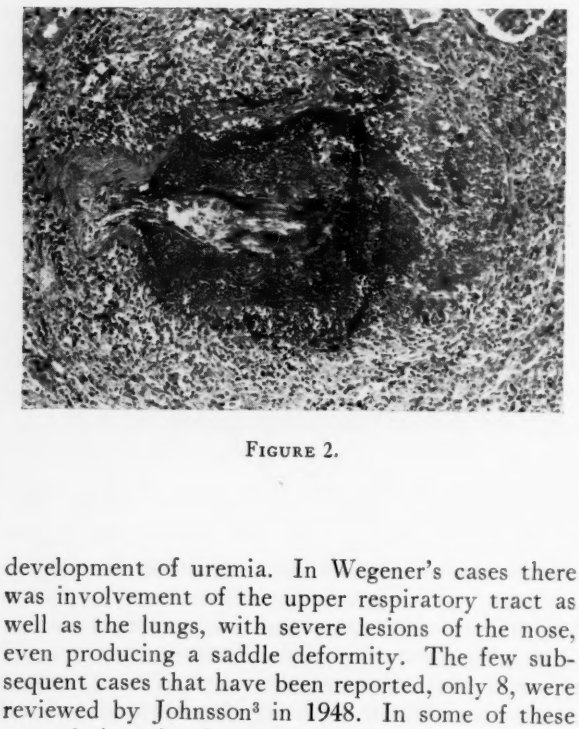

FIGURE 2.

development of uremia. In Wegener's cases there was involvement of the upper respiratory tract as well as the lungs, with severe lesions of the nose, even producing a saddle deformity. The few subsequent cases that have been reported, only 8, were reviewed by Johnsson[3] in 1948. In some of these cases lesions in the upper respiratory tract have been as mild as middle-ear involvement, but the picture in the lungs and in the kidneys has been quite uniform. The lesions in the case under discussion are, I believe, entirely consistent with the granulomatous disease that Wegener described, and that is the diagnosis I have to make. The etiology is totally unknown. It may be closely related to periarteritis nodosa, but there are lesions present that appear to have no connection whatsoever with blood vessels. That seems to make a sharp differentiation, besides the peculiar concentration of lesions in the respiratory tract and kidneys. Other organs in the body may be involved but much less commonly so.

DR. BAKER: May I ask Dr. Wyman if he recognizes any picture in the lung x-ray film that is suggestive of periarteritis nodosa?

DR. WYMAN: This picture is certainly compatible with that diagnosis.

DR. MALLORY: We could not find an arterial lesion in the lung. They were all extravascular there.

DR. QUERIDO: I should like to ask Dr. Mallory whether he found anything in the liver that might be consistent with periarteritis?

DR. MALLORY: Nothing was found in the liver. There were two lesions associated with vessels in the spleen.

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CASE 36382

PRESENTATION OF CASE

First admission. A fifty-year-old man was admitted to the hospital complaining of shortness of breath.

The patient had been seen in the Out Patient Department three years before entry because of palpitations and dyspnea on exertion, which had begun with the onset of severe financial worries eleven years before and had fluctuated considerably in the intervening years, in proportion to his emotional tension. He had taken no previous medication. He could remember only measles among the common childhood diseases and had had diphtheria at the age of twenty-three. He denied scarlet fever, rheumatic fever or venereal disease. A bilateral inguinal herniorrhaphy had been performed. He had nocturia (two times) for the preceding six months. On the initial examination the heart was enlarged with the point of maximum impulse 8.5 cm. to the left of the midline. The pulse was 42 and fairly regular except for occasional short bursts of doubled rate, brought on by exercise. The pulmonic second sound was equal to the aortic and an occasional third heart sound was heard. There were no thrills or murmurs. The blood pressure was 130 systolic, 80 diastolic. There were no engorged cervical veins, no edema and no abnormally palpable peripheral arteries. The retinal vessels showed arteriovenous nicking. When seen in the Out Patient Department three months later he was somewhat worse, with the liver edge palpable 2 cm. below the costal margin and minimal pitting edema of the ankles. The heart was fibrillating at a rate of 130, and the blood pressure was 120 systolic, 80 diastolic. X-ray examination disclosed a generally enlarged heart and some fluid at the lung bases. An electrocardiogram was interpreted as typical of auricular fibrillation, with left ventricular strain, irritable heart

and some evidence of coronary-artery disease. Digitalization brought marked improvement in two weeks' time, and the patient did not return for further follow-up study. In the interval of three years to the first hospital admission he had taken digitalis intermittently and had been comparatively free of symptoms until the last six months, when he began to be bothered by choking sensations on exertion and by increased swelling of the ankles. For two weeks he had had a cough, with rusty and sometimes bloody sputum. There had never been any chest pain.

Physical examination showed a ++++ pitting edema of the legs and a + edema of the sacrum. The lungs were clear. The heart was further enlarged, with the apex 10 cm. to the left. The blood pressure was 180 systolic, 120 diastolic. The sounds were of good quality, but irregular with gallop rhythm and extrasystoles. There was a Grade I mitral systolic murmur. The liver edge was palpated three fingerbreadths below the costal margin.

Examination of the blood revealed a red-cell count of 5,800,000, with a hemoglobin of 16 gm., and a white-cell count of 11,000, with a normal differential. The stools were consistently guaiac negative. The nonprotein nitrogen was 10 mg., and the total protein 6.8 gm. per 100 cc. The blood Hinton test was negative. The vital capacity was 1.7 liters, increasing to 2.3 liters on treatment. Urinalysis showed a specific gravity of 1.016 and a ++ test for albumin. An electrocardiogram disclosed auricular fibrillation at a rate of 85 and marked left-axis deviation, with the ST segment depressed and sagging in Lead 1 and slightly elevated in Lead 3. The T waves were inverted in Lead 1, diphasic in Lead 2 and upright in Lead 3. The tracing was considered to be not significantly changed from the previous examination. The x-ray films were unchanged except for the left auricle, which appeared rather large for simple congestive failure. The patient was discharged after two weeks, much improved, on digitalis and ammonium chloride.

Second admission (seven months later). He had been free of symptoms for a short time and had returned to work. Edema had recurred, but had been controlled by mercurial diuretics three times weekly and some restriction of salt and fluid. Nitroglycerin twice a day relieved him of the choking sensation on exertion. There had been a recent increase in edema and dyspnea.

Physical examination showed cyanosis, marked dyspnea, engorged neck veins, ascites and pulmonary congestion of such severity that he was not expected to recover. On examination the heart was the same as before. X-ray films of the chest indicated a left hydrothorax and pulmonary edema. The blood pressure was 130 systolic, 90 diastolic.

Examination of the blood disclosed a red-cell count of 4,500,000, with a hemoglobin of 13.5 gm., and a white-cell count of 16,200. The nonprotein nitrogen was 30 mg. per 100 cc., and the chloride 103 milliequiv. per liter.

The patient made a remarkable recovery on bed rest, oxygen, venesection, mercurial diuretics and digitalis and was discharged to a rest home after two weeks.

Third admission (three years later). He had returned to work from the rest home. On digitalis, ammonium chloride and a low-salt diet he had remained free of symptoms for two and a half years. During this time he had worked as a salesman, walking all day and carrying a 20-pound sample case. A few months prior to admission the dyspnea and palpitations recurred. Return to regular use of mercurial diuretics gave him relief for a while, but none for the preceding month. In that month he had considerable exertional dyspnea, paroxysmal nocturnal dyspnea and one episode of brief precordial pain. No edema, cough or hemoptysis had been noted.

Physical examination showed the heart to be enlarged. There was a Grade III blowing systolic murmur at the apex. The pulmonic second sound was louder than the aortic. The rhythm was irregular at a rate of 74 without radial deficit. The blood pressure was 180 systolic, 130 diastolic. The liver edge was palpated three fingerbreadths below the costal margin, and there was + ankle edema.

X-ray and laboratory findings were unchanged. The sedimentation rate was 15 mm. per hour. An electrocardiogram showed considerably lower voltage, but was otherwise unchanged.

He again recovered and was discharged in two weeks.

Fourth admission (six months later). He had done well, working again in the interim. For the past three weeks he had had dyspnea and orthopnea, interfering with sleep. In the year prior to admission he had increasing difficulty with the joints, consisting of transient aching in the knees, ankles and shoulders, without redness, tenderness or swelling. During other episodes he had described "weakness in the knees," which had been diagnosed as degenerative arthritis in the Orthopedic Clinic. Extensive inquiry revealed no history suggestive of rheumatic fever previously. He had had cramps in the calves from time to time, presumably on the basis of low sodium, but recognized these as a separate entity.

Physical examination was about the same as on the previous admissions. The apical systolic murmur was now Grade IV and quite harsh. The rhythm was irregular at a rate of 80. A few observers heard a faint mitral mid-diastolic murmur. The blood pressure was 180 systolic, 130 diastolic. There was no edema.

The urine gave a + test for albumin. The hemoglobin was 14 gm. The white-cell count was 13,000, falling to 6000 in several days, with a normal differential. The sedimentation rate was 34 mm. per

hour. He again improved rapidly on the usual cardiac regime, and was discharged after twelve days.

Final admission (two years later), again because of increasing dyspnea. Following discharge he rested for six months and then returned to work. He found however that he could no longer carry the sample case. He was on a low-salt diet, a schedule of digitalis, ammonium chloride and phenobarbital daily, and Mercuhydrin once weekly. Each injection of Mercuhydrin was followed by a twelve-hour diuresis with a 3-pound weight loss and resulted in a subjective feeling of improvement. He continued, however, to be dyspneic on exertion. For eighteen months he had had pain in the right shoulder, treated with physiotherapy as bursitis. There had been a recurrence of his inguinal hernia on the left for one or two years. For the two months before entry he had had intermittent cough. One month prior to admission there had been an increase in the fluid in the chest, and the mercury had been increased to twice a week. For two months he had had a sensation of food, both solid and liquid, sticking in the throat. There had been no nausea or vomiting.

Physical examination showed orthopnea, distended and pulsating neck veins, cyanosis and an irregular pulse without deficit. There was no peripheral edema. Moist rales were heard at both bases. The heart was generally enlarged, and the point of maximum impulse was 12 cm. to the left of the midline. The heart sounds at the apex were obscured by a Grade IV, harsh, blowing systolic murmur, which was transmitted to the posterior axillary line and along the left sternal border. There was a slight apical systolic thrill. A variable Grade II mid-diastolic murmur was heard at the apex, and a phonocardiogram showed mid-diastolic vibrations at the apex that had increased since a reading two years before. The blood pressure was 130 systolic, 100 diastolic. The liver was felt four fingerbreadths below the costal margin, with an indistinct edge. No ascites was found. There was a large recurrent left inguinal hernia containing intestine.

X-ray films showed little change other than increase in the right-sided cardiac enlargement. An electrocardiogram demonstrated no change. The urine had a specific gravity of 1.015 and was otherwise normal. The hemoglobin was 12 gm., and the white-cell count 7600, with 80 per cent neutrophils. The sedimentation rate was 40 mm. per hour, the vital capacity 1.9 liters, and the carbon dioxide 22.7 milliequiv., the chloride 106 milliequiv., the sodium 135 milliequiv., and the potassium 5 milliequiv. per liter, and the calcium 7.8 mg. per 100 cc.

The condition remained fairly stable clinically for several weeks except for an increase in body weight when resin was not being administered and a decrease when it was. The diet contained about 4 gm. of salt, which approximated the daily intake at home. Slight ankle edema formed toward the end of each day but was gone by morning, and moderate dyspnea and orthopnea coming on at the time of retiring disappeared in a short time. There was moderate week-to-week fluctuation by physical examination, with signs of congestive heart failure evident when the weight was high. Six weeks after admission, while resin therapy of 45 mg. per day was being given, a repeat chemical survey showed a nonprotein nitrogen of 56 mg., calcium of 8.6 mg., and phosphorus of 4.6 mg. per 100 cc., and a sodium of 137 milliequiv., chloride of 120 milliequiv., potassium of 3.7 milliequiv. and carbon dioxide of 16.8 milliequiv. per liter.

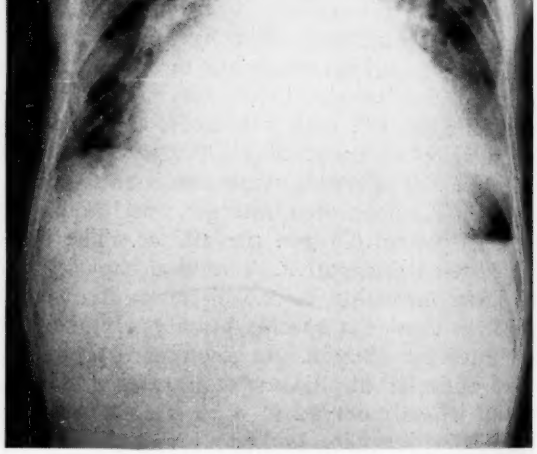

FIGURE 1.

X-ray films demonstrated some increase in heart size (Fig. 1 and 2). An electrocardiogram showed little change except for ventricular extrasystoles.

One week before death, while on resin and potassium acetate, the patient was given 1 cc. of a mercurial diuretic with a prolonged diuresis lasting two days and a loss of 7 kg. of weight. He was relieved of all orthopnea and had no objective evidence of congestive circulatory failure. He did complain of considerable weakness at this time and was disinclined to leave his bed. The vital capacity was 2.3 liters. He was found dead on the morning of the fiftieth hospital day, having been seen awake and apparently normal within the hour.

DIFFERENTIAL DIAGNOSIS

DR. DOROTHEA G. LOOFBOUROW*: To recapitulate, this fifty-year-old-man exhibited considerable

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anxiety when first seen in the Out Patient Department, and this, I believe, obscured the fact that he was at that time on the verge of congestive heart failure. Three months later when he returned the heart was fibrillating at a rate of 120 and was generally enlarged, and there was fluid at the lung bases. Digitalization caused a marked improvement. He was well enough to need little help for three years, at which time he was admitted to the hospital because of congestive failure, mostly right sided. Within two weeks he was discharged, improved, on digitalis and ammonium chloride. It is of interest that although he had not been expected to live before treatment, he responded well to the usual remedy for congestive failure. In the light of subsequent events this observation seems important. From this point on he was admitted to the hospital at intervals varying between six months and three years for congestive heart failure, most of which appeared to be left-sided failure. On the whole he did well for a patient in recurrent congestive heart failure.

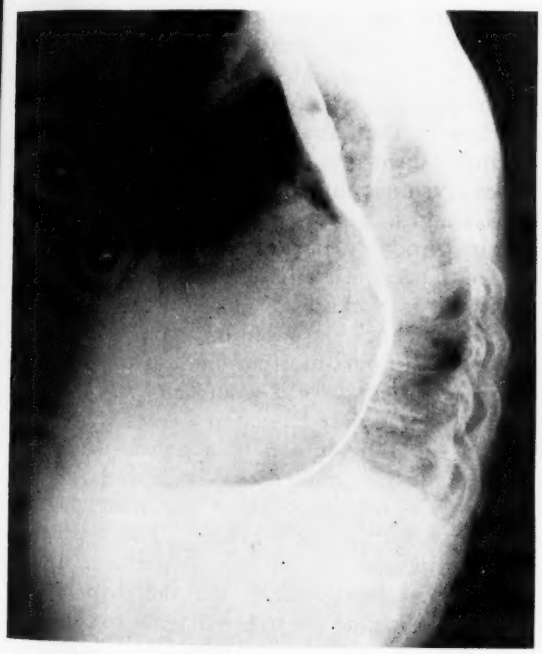

FIGURE 2.

In the year before the fourth admission, there was a change in the general picture consisting of involvement of the skeletal system by transient aching in several joints. The history of migratory joint involvement in addition to an elevation of the white-cell count and sedimentation rate (the temperature is not mentioned in the protocol) is consistent with rheumatic fever. The patient was discharged only twelve days after the fourth admission, but arrangements were made for him to rest for six months. If my interpretation is correct, I suspect that the diagnosis on discharge in addition to the usual one of congestive heart failure was active rheumatic fever.

At the last admission two years later he had developed auscultatory signs, which were consistent with deformity of the mitral valve — a Grade IV, harsh, systolic murmur and a variable mid-diastolic murmur at the apex. A phonocardiogram showed mid-diastolic vibrations, which had increased in two years. This is supposed to confirm the finding of a sound that can be heard by auscultation if one's ears are good enough. At this final admission the patient was very ill, but from the protocol I believe that he had been as ill at the time of his first admission years before. He had distended neck veins and a very large heart that apparently was large in all areas. The heart was fibrillating, and there were moist rales at the bases. The liver edge was palpated four fingerbreadths below the costal margin, but this does not necessarily mean that the liver was enlarged.

Could we look at the x-ray films, Dr. Wyman?

DR. STANLEY M. WYMAN: The earliest films taken about five years before the final entry show the greatest change to be in the region of the left ventricle, with very little prominence of the left auricle. The hilar and pulmonary-vessel shadows are only very slightly increased in prominence. Six months later the patient has obvious left pleural effusion, severe congestive changes in both lungs and pulmonary edema in all probability. The next films, taken three years later, show a slight further increase in the size of the left ventricle, but at this time there is also a definite enlargement of the left auricle posteriorly. The hilar and pulmonary vascular shadows are more prominent than previously so that there is probably an increase in the pulmonary congestion. The next examinations, two years later, show still more increase in the heart size, particularly involving the left auricle, which extends far posteriorly, spreads the carina very markedly and compresses the esophagus against the spine and against the aorta, probably accounting for the difficulty in swallowing and the complaint of food sticking in the throat. The hilar and pulmonary-vessel shadows have become still more prominent, and one month later there is still further increase in their size, with possibly some degree of pulmonary edema at that time. The last set of films (Fig. 1 and 2) show some improvement in pulmonary congestion, but there is still further increase in the size of the enormous left auricle. By this time all chambers appear enlarged. There is no note anywhere in the record, as far as I am aware, of calcification in the region of the valves.

DR. LOOFBOUROW: I suspect that during the last admission it had become difficult to control the congestive heart failure. That would explain the

vigorous attempt that was made to rid the patient of sodium ions. This was done by several methods. The intake of sodium was limited to 4 gm.; ammoniated cation resin and potassium acetate were both given orally, although the potassium would have had little effect since it would have been adsorbed by the resin; and finally one week before death 1 cc. of a mercurial diuretic was given. Whether the patient was on ammonium chloride or not I do not know because it was not specifically stated.

Because of the recent use of exchange resins I might take a few minutes to give a little historical background about the development of exchange resins. This is one of the several methods used for separation of materials, all of which come under the general name of chromatography. During the 1930's the method was used by Kuhn[1] and others to separate plant pigments on columns containing adsorbing substances, and the field comprising the several methods of chemical separation at that time was given the general name of chromatography because of the color of plant pigments such as chlorophyll and carotene. A weak cation or anion adsorbed on an appropriate resin will be replaced, in part, by any stronger cation or anion if these come in contact with the resin; hence the name "ionic exchange" resins. The use of such resins was highly developed during World War II as a means of separating the rare earths and atomic-pile fission products.

The rationale of the use of resins in congestive heart failure is based on the fact that a suitably treated cation-binding resin will take up large quantities of sodium ions and thus will reduce the amount of sodium ions in the body. However, it should be pointed out that cation-exchange resins are not specific for sodium, but adsorb cations of all kinds, including calcium, potassium, magnesium and barium. Indeed, the affinity of ammoniated cation resin for potassium is greater than that for sodium (Kressman and Kitchener[2]). Furthermore, when sodium is taken up from sodium chloride by a cation-exchange resin, free chloride ions are released. Irwin et al.[3] found a reduced absorption of sodium and potassium from the gut in the presence of a relatively constant absorption of chlorides, phosphates and sulfates when resin was administered. The mechanism of acidosis induced by resin is thus explained, for this results in an excess of anions and a concomitant decrease in cations. In the case described by Irwin and his associates, as the resin administration progressed, the plasma carbon dioxide combining power fell from 27 to 19 milliequiv. per liter and the chloride rose from 102 to 112 milliequiv. per liter with no significant change in the pH of the blood. There was no kidney impairment in the case discussed by them and sulfates were balanced by the formation of ammonia that increased from 25 to 211 milliequiv. per day on the thirty-fourth day.

In the case under discussion the carbon dioxide combining power fell from 31.4 to 16.8 milliequiv. per liter, and the chloride rose from 102 to 120 milliequiv. per liter. There was evidence of some renal impairment, and it may be assumed that the balancing of the excess anion by increased formation of ammonia did not take place very efficiently. Acidosis therefore resulted. The chemical findings before resin therapy were a carbon dioxide of 31.4 milliequiv., chloride of 102 milliequiv., sodium of 135 milliequiv. and potassium of 5.5 milliequiv. per liter, and a calcium of 9.4 mg. and phosphorus of 3.7 mg. per 100 cc. After six weeks the respective figures were 16.8 milliequiv., 120 milliequiv., 137 milliequiv., and 3.7 milliequiv. per liter and 8.6 mg. and 4.6 mg. per 100 cc. From a comparison of these figures it is obvious that the patient was acidotic after resin therapy — carbon dioxide was well within the levels considered acidotic, and the chloride was very high. The resin prevented little if any absorption of cation from the gastrointestinal tract, but liberated anions were absorbed in the usual quantities. Following resin therapy, when the patient was already acidotic, he was given mercury, which resulted in a prolonged diuresis and a loss of 15 pounds in two days. The mercury probably pushed out more sodium, causing him to become even more acidotic. In that event the immediate cause of death would have been acidosis or shock or a combination of both. This would give no post-mortem findings to substantiate the cause of death, for it would be a so-called "clinical death." He may have had a coronary occlusion, which is not uncommon in a person whose blood pressure has been reduced to shock levels.

I am quite uncertain about the underlying cause of the congestive heart failure. The hypertension does not impress me as very important. The history of joint involvement and the shape and size of the heart incline me to the diagnosis of rheumatic heart disease, with involvement of the mitral and aortic valves. Probably, there was emphysema, a cardiac cirrhosis, a recurrent left inguinal hernia and some damage to the kidneys.

Dr. Jacob Lerman: At the time of the first admission the Service believed that the patient had straightforward hypertensive heart disease, generalized arteriosclerosis, with auricular fibrillation, and very severe congestive heart failure. At that time it seemed that the prognosis was very poor, but he lived for seven years following that episode. The question of rheumatic heart disease was raised in discussion on the basis of the x-ray findings, but clinically it could not be confirmed. All we could hear was a short, Grade II, systolic murmur, which had decreased in the years following. It raised the possibility that this was all due to hypertensive heart disease with marked dilatation of the mitral valve and relative mitral regurgitation, producing the subsequent findings in the left auricle.

DR. AUSTIN L. VICKERY: There seems to be a considerable difference of opinion among the various clinical observers about whether this man had hypertension or not.

DR. LERMAN: The various blood-pressure readings on the first and second admissions were all in the neighborhood of 180 and 200. There were times when it was a little lower.

CLINICAL DIAGNOSIS

?Rheumatic heart disease.
?Hypertensive heart disease.

DR. LOOFBOUROW'S DIAGNOSES

Acidosis — probably resulting from resin therapy.
Rheumatic heart disease with involvement of mitral valve, ?aortic valve.
Emphysema.
Cardiac cirrhosis.
?Kidney disease.

ANATOMICAL DIAGNOSES

Idiopathic cardiac hypertrophy.
Cardiac dilatation, marked.
Hydropericardium.

PATHOLOGICAL DISCUSSION

DR. VICKERY: On the death certificate the first clinical diagnosis was listed as rheumatic heart disease, and the second as hypertensive heart disease.

At autopsy the pericardial sac contained about 150 cc. of clear, yellow fluid. The heart weighed 605 gm. and was enormously dilated, with the generalized hypertrophy shared rather equally by both right and left sides; the left ventricular wall averaged about 2 cm. in thickness, and the right almost 1 cm., so that both ventricles were approximately twice the normal thickness. On section the myocardium proper showed a normal homogeneous rich reddish-brown color. No areas of old or recent infarction could be discerned. The coronary arteries were widely patent. There was no significant degree of atherosclerosis. The valve rings were all dilated. There was no thickening of the valve leaflets or of the chordae tendineae and no calcification of any of the valve rings. Microscopically, we did not learn much more. There was a slight diffuse interstitial fibrosis of the myocardium and a few focal areas of scarring, probably on the basis of relative anoxemia. Nothing was evident to indicate a recent or old active myocarditis of an infectious nature, and there was nothing to indicate a recent or old massive zone of infarction. That was just about as far as we could go.

The remainder of the autopsy was quite unremarkable. The aorta demonstrated a moderate degree of atherosclerosis. The lungs were fluffy and light, weighing 720 gm. They showed no evidence of fibrosis. The patient did not die in an attack of acute congestive heart failure, and there was little in the lungs to indicate that he had much long-standing congestive failure. There was only very slight emphysema. The liver revealed some chronic passive congestion, as did the spleen. The kidneys showed a moderate degree of sclerosis.

The etiology of the cardiac hypertrophy seemed to be in the order of so-called idiopathic cardiac hypertrophy.[4] The degree of both right and left ventricular hypertrophy was entirely out of proportion to the clinical evidence of hypertension. Certainly, there was nothing to incriminate the coronary arteries, and for lack of any better classification, that is how this case was classified. We have had a fair number of such cases in the past, 2 of which were rather dubious with question marks by them. The entity is most frequent in infants and in young children, in whom it is called congenital idiopathic hypertrophy. The hearts are often twice or three times the normal size, frequently the result of abnormal glycogen storage. In adults, however, the explanation is not quite so easy.

DR. WALTER BAUER: Why not call it chronic myocarditis? Why call it idiopathic cardiac hypertrophy?

DR. VICKERY: It depends on the academic definition of myocarditis. If one defined myocarditis as a diffuse increase in the interstitial tissue without any evidence of active inflammation in the wall, the name would be appropriate.

DR. JAMES H. CURRENS: Some of the chemical determinations on tissue taken at autopsy might be mentioned. Analysis of the electrolytes of the heart and the psoas muscles demonstrated a relatively low ratio of potassium to sodium. In the myocardium the ratio of potassium to sodium was 40 to 56 milliequiv. per kilogram of wet tissue. In the psoas muscles, the ratio was 70 milliequiv. of potassium to 40 milliequiv. of sodium, so that there was quite a profound difference between the ratios of the two cations in the cardiac and skeletal muscles. It is interesting to speculate about whether the low potassium content of the cardiac muscle was primary or secondary to the prolonged cardiac failure.

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COUNCIL ON NATIONAL EMERGENCY MEDICAL SERVICE

THE second regional meeting of the Council on National Emergency Medical Service of the American Medical Association was held at the Hotel Statler in Boston on Sunday, August 27, under the chairmanship of Dr. James C. Sargent. The purpose of the meeting was to stimulate interest and activity first in civil defense and secondly in the procurement of medical officers for the armed forces.

The meeting was well attended; not only were several members of the Council on Medical Service present, but also representatives of the medical societies of the New England states, the American Dental Association, the Red Cross, the Association of American Medical Colleges, the Council of the New England Medical Societies and the Massachusetts Hospital Association.

On the national level representatives were present from the National Security Resources Board, the Office of the Secretary of Defense, the Department of the Army and the Headquarters of the First Army, the Department of the Navy, the First Naval District, the Department of the Air Force, the United States Public Health Services and the National Headquarters of the Selective Service.

Civil defense, in which the stage of detailed tables of organization has been reached, will be almost entirely a civilian project with the primary responsibility centered in the National Security Resources Board. The military department will be able to render only secondary assistance, in case of an emergency of such magnitude that the civilian defenses break down; the hope is that the civilian services may be so well organized that this point cannot be reached.

The demands that major rescue work may make upon the resources of an area can be imagined but hardly calculated on the basis of 250,000 to 300,000 pints of blood being needed in the case of a catastrophe such as that which struck Hiroshima. In effective preparedness such problems as the indoctrination of the population in radiation detection and first aid, the elimination of state boundaries as barriers to competent relief work, and a nationwide uniformity of records must be considered. All these factors have their place in the admirable defense organization already set up in the state of Maine.

The matter of procurement of medical personnel for the armed forces was freely discussed at this meeting as it has been elsewhere, and will presumably have been settled by appropriate legislation prior to the publication of these comments.

ANNIVERSARY OF THE ARMY MEDICAL DEPARTMENT

AS PART of a series of reports on fifty years of progress in various departments of medicine that are planned for publication in the *Journal* next year, one on the advances that have been made in military medicine is in preparation. The authors are Colonel Tom F. Whayne and Colonel Joseph

McNinch, of the Medical Corps of the United States Army, and it is hoped that military exigencies will not deprive them of the time necessary to complete this interesting and useful document.

In view of the proposed report it is noteworthy that the Medical Department of the Army is this year celebrating its one hundred and seventy-fifth anniversary, having been established practically in the streets of Boston in July, 1775. In that month a group of civilian doctors volunteered their services to care for the patriot wounded of the beleaguered city, and on July 27 Congress, at the request of General Washington, approved the creation of a Hospital Department of which Dr. Benjamin Church, of Boston, became the first director general. It was not until nearly a year later that the country became an independent nation.

The personnel of the Army Medical Department, in its hundred and seventy-five years of existence, has made many contributions, some of them outstanding, to the progress of medicine. The contentious Benjamin Waterhouse, a one-time army surgeon despite the fact that even in Revolutionary days medical officers were supposed to be noncombatant, introduced vaccination to the United States.

John Tilton, as surgeon general in 1814, directed hospital surgeons to observe and record the weather; with easy versatility he became the first chief signal officer of the Army, in addition to founding the Weather Bureau. William Beaumont was a medical officer in the Regular Army when he made his observation on gastric secretion, and Surgeon Jonathan Letterman during the Civil War organized an ambulance service that has remained a model even for the armies of today.

Surgeon John S. Billings, who devised the Index Catalogue of the Army Medical Library, designed both the Johns Hopkins and the Peter Bent Brigham hospitals and made contributions to the science of ventilation; the work done by Major Walter Reed and his commission in demonstrating the relation between the mosquito and yellow fever, and Colonel Gorgas's application of this knowledge in making a health resort of the Panama Canal Zone are too well known to need repetition.

It was the Army Medical Department that added so much to the knowledge of typhoid fever during the Spanish-American War, and a chemist at the Army Medical School invented the first apparatus for the chlorination of water.

When to these contributions are added the vast array of more recent advances that have been made along a solid front of science during the period encompassed by the two world wars, the contributions of the Department to civilian as well as to Army health can be appreciated.

THE PSYCHOPATHIC OFFENDER

ENGLAND, looking down the trail that has been blazed in Denmark, has studied the matter of the treatment that should be accorded mentally abnormal criminals who are nevertheless not insane. The Home Secretary's Advisory Council on the Treatment of Offenders, whose report appeared in the *Lancet* on June 17, favors a special penal institution for these psychopathic felons, somewhat like the famous prison at Herstedvester described in an editorial in the *Journal* on July 7, 1949.

The use of the proposed institution would be for criminals guilty of an offense calling for a prison sentence of at least four months, considered to be the shortest time in which any psychotherapy might be of value. Those guilty of less serious crime would be treated voluntarily by probation and outpatient psychotherapy. The Home Secretary or the Prison Commissioners, according to the recommendation of the Advisory Council, would have the authority to transfer prisoners to or from the institution; Courts of Quarter Sessions and Assizes could order periods of treatment in it, although, with inflexible British justice, the period of special detention could not be longer than the maximum sentence prescribed by law for the particular offense. The offender, in other words, would receive the sentence established by law for that crime, not an indefinite commitment for the treatment of a condition that made him a dangerous person to have at large.

The *Lancet* in the following week, June 24, reported also on the documentary film taken in Denmark's psychopathic prison at Herstedvester, which had been shown at the Institut Français by Dr.

Georg Stürup, director of the prison. The characteristics of the psychopath are brought out in the film — "the over-determined gait, the over-manly chewing of the pipe and furrowing of the forehead, the egocentricity, the petty lies and silly sulks, the lack of facial mobility."

In contrast to the present possibilities in England, it is Dr. Stürup's conviction that the indeterminate sentence is the most important part in the nearly 50 per cent success rate in reforming those adults who refuse to grow up. The desire to improve comes with the realization that they cannot get out until they have shown their ability to live at peace with Society. "Without this fierce stimulus the psychopath will make no effort to grow up and face the world as it is."

The sexual psychopath, as was previously stated, is usually castrated as a condition of release, and occasionally even these *castrati*, cured and given their liberty, will marry happily and successfully, often to divorced women who have had "more than enough of sex with their previous husbands." Better than making the punishment fit the crime is making the treatment cure the criminal. Perhaps such enlightened penology will some day receive serious consideration in all the democratic countries.

THE FIRST HUNDRED ARE THE HARDEST

THE Massachusetts district medical society centenary season will close on October 2. On that date the Middlesex South and the Plymouth district societies, the fourteenth and fifteenth of the Massachusetts Medical Society component group to be incorporated, will observe their hundredth birthdays, the third and fourth to be so celebrated this year. From that point on the going is expected to be easy.

Middlesex South, whose committee is under the chairmanship of Dr. H. Quimby Gallupe, will dine on the appointed day at the Hotel Continental in Cambridge. Dr. Roger I. Lee will be the guest speaker of the evening, and a souvenir program and historical exhibit has been prepared by Dr. Robert W. Buck.

The Plymouth district society will celebrate the end of this first stage in its slow journey toward longevity also with a dinner meeting to be held at Harris Hall in North Plymouth. The occasion will mark in addition the first anniversary of the Woman's Auxiliary of the Society. Dr. Arthur W. Allen will be the principal dinner speaker, and the guests will include Mrs. Allen, Dr. and Mrs. Howard F. Root, Mrs. Root representing the Woman's Auxiliary of the Massachusetts Medical Society, and Dr. and Mrs. John F. Conlin.

The significance of Plymouth Rock will no doubt be borne in mind even if White Rock in its various combinations seems at the moment to be in the ascendant.

The following remarks we find in the St. Louis Probe: — "*The plan of attending families by the year is dictated by a trading mercenary spirit, unworthy of members of a dignified profession...*"

Boston M. & S. J., *Sept. 18, 1850*

MASSACHUSETTS MEDICAL SOCIETY

STATED MEETING OF THE COUNCIL

A stated meeting of the Council will be held in John Ware Hall, Boston Medical Library, 8 Fenway, Boston, on Wednesday, October 4, at 10:30 a.m. This meeting will be followed by the Cotting Luncheon.

Business:

1. Presentation of record of Annual Meeting of the Council held May 15, 1950, as published in the *New England Journal of Medicine*, issue of July 27, 1950.
2. Reports of standing and special committees.
3. Such other business as may lawfully come before the meeting.

H. QUIMBY GALLUPE, M.D., *Secretary*

DEATHS

FLETCHER — Robert S. Fletcher, M.D., of Oxford, died on September 3. He was in his seventy-ninth year.

Dr. Fletcher received his degree from Jefferson Medical College of Philadelphia in 1901. He was formerly school physician and chairman of the Board of Health in Oxford and was a fellow of the American Medical Association.

A daughter survives.

JANTZEN — Francis T. Jantzen, of Boston, died on June 12. He was in his sixty-fifth year.

Dr. Jantzen received his degree from Harvard Medical School in 1908. He was a member of the staffs of Carney, Boston City and St. Elizabeth's hospitals and was a fellow of the American College of Surgeons and American Medical Association.

His widow, four sons and a daughter survive.

BOSTON MEDICAL LIBRARY

SEVENTY-FIFTH ANNIVERSARY

On October 18, 1950, the Boston Medical Library will celebrate the seventy-fifth anniversary of its foundation. Two ground-floor rooms on Hamilton Place were opened as a library, for the use of Boston physicians, on Monday, October 18, 1875, with James Read Chadwick as librarian, E. H. Brigham as assistant librarian in charge and Oliver Wendell Holmes as president of the new association. The present building was occupied in 1900. Long associated with the Library are the *New England Journal of Medicine* and, more recently, the *Journal of Bone and Joint Surgery*. The Massachusetts Medical Society, at present housed in the building, has this year acquired the adjacent property as a permanent home.

To mark its birthday, the Library will hold "open house" on October 18, with a scientific session and a dinner.

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

LABORATORIES APPROVED FOR PREMARITAL AND PRENATAL BLOOD TESTS

On the basis of the evaluation of serologic tests for syphilis for 1949–1950, thirty-four laboratories have been granted approval for diagnostic tests to August 8, 1951. Only laboratories that are approved by the Department of Public Health for diagnostic serologic tests for syphilis may legally perform the *premarital* and *prenatal* blood tests required by law. The Wassermann Laboratory is the only laboratory in Massachusetts whose reports for premarital purposes are recognized in other states.

In addition to the Wassermann Laboratory, 281 South Street, Jamaica Plain 30, the approved laboratories are as follows:

Location	Laboratory
Boston	Boston Dispensary
	Boston Health Department
	Commonwealth Clinical Laboratory
	Leary Laboratory
	Massachusetts General Hospital
	Massachusetts Memorial Hospitals, Genito-Infectious Disease Clinic
Brockton	Brockton Board of Health
Brookline	Sias Laboratories
Clinton	Clinton Hospital
Fitchburg	Burbank Hospital
Great Barrington	Fairview Hospital
Haverhill	Hale Hospital
Holyoke	Holyoke Hospital
	Providence Hospital
Lawrence	Lawrence General Hospital
Lowell	Lowell General Hospital
Montague City	Farren Memorial Hospital
New Bedford	Burt Laboratory
	St. Luke's Hospital
Newton	Newton–Wellesley Hospital
North Adams	North Adams Hospital
Norwood	Norwood Clinical Laboratory
Pittsfield	Pittsfield General Hospital
	St. Luke's Hospital
Quincy	Quincy City Hospital
Salem	Salem Hospital
Springfield	Mercy Hospital
Tewksbury	Tewksbury State Infirmary
Waltham	Waltham Hospital
Westfield	Noble Hospital
Worcester	St. Vincent Hospital
	Worcester City Hospital
	Worcester Hahnemann Hospital
	Worcester Health Department

CONSULTATION CLINICS FOR CRIPPLED CHILDREN IN MASSACHUSETTS

The October schedule for Consultation Clinics for Crippled Children in Massachusetts under the provisions of the Social Security Act follows:

Orthopedic Clinics	Date	Clinic Consultant
Salem	October 2	Paul W. Hugenberger
Haverhill	October 4	William T. Green
Greenfield	October 5	Charles L. Sturdevant
Lowell	October 6	Albert H. Brewster
Gardner	October 10	Carter R. Rowe
Springfield	October 17	Garry deN. Hough, Jr.
Pittsfield	October 18	Frank A. Slowick
Brockton	October 19	George W. Van Gorder
Worcester	October 20	John W. O'Meara
Fall River	October 23	David S. Grice
Hyannis	October 26	Paul L. Norton

Rheumatic Fever Clinics	Dates
North Reading	October 3, 10, 17, 24, 31
Fitchburg	October 4, 11, 18, 25

Plastic Clinics	Consultant
Eastern Massachusetts	Bradford Cannon
Semi-monthly	
Western Massachusetts	Joseph M. Baker
Monthly	

Physicians referring new patients to clinics should get in touch with the district health officer to make appointments. Patients are seen by appointment only.

BLUE CROSS-BLUE SHIELD

NEW SERVICE-BENEFIT CATEGORY FOR BLUE SHIELD

The Blue Shield program as revised to include a new service-benefit category for individuals and families with annual incomes of $5000 or less has been approved by the Department of Insurance.

Although an effective date of September 1, 1950, has been established so that benefits for surgical services rendered by oral (dental) surgeons to hospitalized bed patients may be provided immediately, existing contracts will not be replaced until January, 1951, for the reason that it will take several months to acquaint all subscribers currently in the over-income bracket with the advantages of the $5000 income-limit plan.

Between now and December 1, 1950, most new subscribers will be enrolled under the present Blue

Shield plan, with the understanding that those who want the $5000 income-limit plan may have it beginning in January, 1951. Exceptions will be made in the case of large groups for which a subsequent adjustment would pose serious administrative and educational problems.

In the near future a new Blue Shield manual, including rules and regulations and schedules of fees, will be sent to all participating physicians.

CHARLES G. HAYDEN, M.D.
Executive Director

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

A Twentieth Century Physician: Being the reminiscences of Sir Arthur Hurst, D.M., F.R.C.P. With a foreword by Professor John A. Ryle, M.D., F.R.C.P. 8°, cloth, 200 pp., with 11 plates and frontispiece. Baltimore: Williams and Wilkins Company, 1949. $3.50.

Sir Arthur Hurst, a graduate of Oxford and at one time physician at Guy's Hospital, London, and leading medical consultant, retired in 1939. He died in 1944. He wrote his autobiography in the period after his retirement. He did not keep diaries, but depended on his remarkable memory, supplemented by letters and documents. Trained in the Oxford school of physiology, he was one of the first to foster the regular application of physiologic principles and methods to bedside problems. He was always alert to new ideas and methods in medicine. In 1919 he established the New Lodge Clinic for psychoneurotics. He traveled much, on the continent and abroad, visiting the United States in 1919. His life story was left unfinished at his death, but with the help of Lady Hurst, his reminiscences have been preserved in this delightful volume.

External Morphology of The Primate Brain. By Cornelius J. Connolly, Ph.D., professor of physical anthropology, Catholic University of America, Washington, D. C. 8°, cloth, 378 pp., with 337 illustrations. Springfield, Illinois: Charles C Thomas, 1950. $10.00.

In this monograph the author gives the results of his studies on the development of cortical fissuration of the primate brain, from the lemur to man. Some of the material was published originally in the *American Journal of Physical Anthropology*. This material has been revised and amplified with new studies. Nearly a hundred pages of text are devoted to the human brain of the newborn, children and adults. There is a bibliography but not an index. The volume is an excellent example of fine publishing. It should be in all anatomic and neurologic collections.

Optics. By Arthur Linksz, M.D., Manhattan Eye, Ear and Throat Hospital, University Hospital and New York University College of Medicine. With a foreword by Walter B. Lancaster, M.D. Vol. I. *Physiology of the Eye.* 4°, cloth, 334 pp., with 137 illustrations. New York: Grune and Stratton, 1950. $7.50.

The contemplated treatise on physiology of the eye will be published in three volumes, on optics, physiology of vision, and biochemistry of the eye. The present volume on optics is divided into three main sections: physics of light; geometric optics; and the eye as an image-forming mechanism. The book is well published and should be in all collections on ophthalmology.

Breast Deformities and Their Repair. By Jacques W. Maliniac, M.D., clinical professor of plastic reparative surgery and associate attending plastic reparative surgeon, New York Polyclinic Medical School and Hospital, and attending plastic surgeon, Sydenham Hospital, New York City. 8°, cloth, 193 pp., with 119 illustrations. New York: Grune and Stratton, 1950. $10.00.

This special monograph of particular interest to plastic surgeons covers its subject thoroughly. Bibliographies are appended to the various chapters, and the publishing is excellent. The large number of full page plates and the anticipated small distribution evidently explain to some extent the comparatively high price for this monograph. The current tendency in medical publishing of issuing a multitude of small monographs will naturally lower distribution. The book should be available to all surgeons interested in breast repair.

The Question of Lay Analysis: An introduction to psychoanalysis. By Sigmund Freud. Translated by Nancy Procter-Gregg. With a foreword by Ernest Jones, M.D. 12°, cloth, 125 pp. New York: W. W. Norton and Company, Incorporated, 1950. $2.50.

This English translation of an important monograph by Dr. Freud presents the case of lay analysis in all its aspects. The small volume should be in all collections on psychoanalysis.

Medicine of the Year. Editorial direction: John B. Youmans, M.D., dean, School of Medicine, Vanderbilt University. 4°, cloth, 204 pp. Philadelphia: J. B. Lippincott Company, 1950. $5.00.

This second issue of a progress series covers general medicine, surgery and the specialties. Twenty-two physicians contributed to the volume. The articles are timely and bring their various fields up to date in the important advances made in medicine since the publication of the first series in 1949. The publishing is excellent. The use of a soft nonglare paper and large type are notable, but the size of the volume is cumbersome. Publishers should give some thought to the bookshelves of libraries and physicians.

Current Therapy 1950: Latest approved methods of treatment for the practicing physician. Editor, Howard F. Conn, M.D. 4°, cloth, 736 pp. Philadelphia: W. B. Saunders Company, 1950. $10.00.

This valuable summary of current methods of treatment is the work of over 250 contributors. The text is divided into fifteen main sections covering the whole field of medicine. It supplements the first volume, published in 1949. There is a comprehensive index, and the publishing is excellent. The book should prove very useful to the practicing physician since it assembles in a single volume the cream of the current literature on treatment.

Mitchell-Nelson Textbook of Pediatrics. Edited by Waldo E. Nelson, M.D., professor of pediatrics, Temple University School of Medicine, and medical director of Saint Christopher's Hospital for Children, Philadelphia. With the collaboration of sixty-three contributors. Fifth edition. 4°, cloth, 1658 pp., with 426 illustrations. Philadelphia: W. B. Saunders Company, 1950, $12.50.

First published in 1933 and last in 1945, this standard textbook has been thoroughly revised and brought up to date. Material has been added, and many sections have been entirely rewritten. Although called a textbook the volume is essentially a treatise and an outstanding reference source on pediatrics. The book is well published in every way. The price is surprisingly low for such a large volume. It is recommended for all medical libraries and to the general practitioner.

Urologic Roentgenology. By Miley B. Wesson, M.D. Third edition. 8°, cloth, 282 pp., with 284 illustrations. Philadelphia: Lea and Febiger, 1950. $7.50.

This compact book is concerned primarily with clinical diagnosis confirmed by roentgenologic findings and proved at operation or by autopsy. The text has been rewritten and

brought up to date. Illustrations have been added so that practically all urologic conditions are depicted. There are lists of appropriate references throughout the text, and a good index. The illustrative work is good, and the publishing is excellent.

Brucellosis (Undulant Fever): Clinical and subclinical. By Harold J. Harris, M.D. With the assistance of Blanche L. Stevenson, R. N., and with a foreword by Walter M. Simpson, M.S., M.D. 8°, cloth, 617 pp., with 111 illustrations. New York: Paul B. Hoeber, Incorporated, 1950. $10.00.

When the author published the first edition of his monograph in 1941, it was based on a study of 250 cases of brucellosis seen between 1932 and 1941. In this second edition, about 450 additional cases have been studied, making a total of approximately 700 cases. The text has been thoroughly revised and brought up to date. The author's experience with Navy personnel has been included in his studies. There is an extensive bibliography and a good index. The monograph is essentially a new work and should supersede the first edition.

The 1949 Year Book of Drug Therapy (November, 1948-October, 1949). Edited by Harry Beckman, M.D., director, Department of Pharmacology, Marquette University School of Medicine. 12°, cloth, 718 pp., with 133 illustrations. Chicago: Year Book Publishers, Incorporated, 1950. $4.75.

This new yearbook covers the whole field of medicine. It is well printed and should prove useful as a reference work.

The Sexual Perversions and Abnormalities: A study in the psychology of paraphilia. By Clifford Allen, M.D., M.R.C.P., D.P.M., physician in charge of the Psychiatric Department of the Seamen's Hospital, Greenwich, and psychiatrist to the Ministry of Pensions, London. Second edition. 8°, cloth, 346 pp. New York: Oxford University Press, 1949. $5.00.

Dr. Allen has written a compact, sound, authoritative book on a condition not usually discussed in society. His text is based on a large experience, and he approaches the subject from a biologic and clinical viewpoint. He outlines the method of treatment he uses in cases of paraphilia. The volume is well published in the customary Oxford style. It should be in all collections on the subject.

Community Health Organization. By Ira V. Hiscock, M.P.H., Sc.D., chairman, Department of Public Health, Yale University School of Medicine. Fourth edition. 8°, cloth, 278 pp. New York: Commonwealth Fund, 1950. $2.75.

First published in 1927 this standard teaching and reference textbook has been revised and brought up to date. It covers general planning, organization, and administration, and includes a discussion of finances. The publishing is excellent, and the book should be in all public-health collections.

Progress in Clinical Endocrinology. Edited by Samuel Soskin, M.D., director, Medical Research Institute, Michael Reese Hospital, Chicago, dean, Michael Reese Hospital Post-Graduate School, and professorial lecturer in physiology, University of Chicago. 8°, cloth, 641 pp. New York: Grune and Stratton, 1950. $10.00.

This progress report on an important field in medicine is the joint work of over 90 contributors. The text is divided into thirteen sections and covers the whole field of clinical endocrinology. The editor has done his work well in producing a smooth, well written, homogeneous presentation of the subject, not an easy task with a large number of writers. Progress reports are becoming more prevalent in English in recent years and, if well done, provide an easy way of keeping up with the multitudinous mass of medical and scientific literature in any particular field of knowledge. This report is excellent. The chapters are documented with lists of references for further reading, and the publishing is good. The volume should be in every medical library and should be available to all physicians interested in endocrinology.

Annual Review of Physiology: Cumulative Index, Vol. I to X. Edited by V. E. Hall, 8°, cloth, 439 pp. Stanford, California: Annual Reviews, Incorporated, 1949. $6.00.

The *Annual Review of Physiology* is now in its twelfth volume. It is an important series of progress reports, and the publishers have provided a valuable general subject-and-author index to the first ten volumes. This volume should be purchased by all libraries and individuals possessing the set. This review is one of seven such publications issued by Annual Reviewers, Incorporated. The others are on biochemistry (nineteen volumes), microbiology (four volumes) and reviews on medicine, plant physiology, and physical chemistry, all beginning with Vol. 1, 1950. The review on medicine might well be dispensed with because the subject is adequately covered elsewhere.

Angina Pectoris and Myocardial Infarction: With special reference to the autonomic nervous system. By Heymen R. Miller, M.D., attending physician, Sydenham Hospital, assistant professor of medicine, New York Postgraduate Medical School and Hospital, and associate attending physician, Montefiore Hospital. 8°, cloth, 336 pp., with 63 illustrations. New York: Grune and Stratton, 1950. $8.75.

The first edition of this monograph was published in 1939 and reissued in 1942. The present edition has been rewritten extensively and revised to date. Chapters on the general functions of the autonomic nervous system, on the autonomic regulation of the circulation and on the anatomy of the peripheral pathways have been added. The text furnishes a survey of the important literature on the subject and the chapters are documented with lists of essential references. There are indexes of authors and subjects, and the publishing is excellent. The monograph is recommended for all medical libraries and for all physicians interested in diseases of the heart.

Grundriss der Allergie: Theorie und Praxis. By Dr. Med. Rudolf Abderhalden. 8°, cloth, 179 pp., with 8 illustrations. Basel: Benno Schwabe and Company, 1950. Gebunden Fr. 14.50.

This manual on allergy is well written, and the text is divided into two sections, general and special. The special section is broken down into the various systems and organs of the body. The bibliographies appended to the chapters are extensive as a rule, and make the manual a good reference tool. The up-to-date list of allergic tests is especially valuable. The publishing is excellent, and the book should be in all collections on the subject.

Medical Diseases of the Kidney (A[illegible]as and Introduction). By J. F. A. McManus, M.D., associate professor of pathology, Medical College of Alabama, Birmingham. 4°, cloth, 176 pp., with 100 illustrations. Philadelphia: Lea and Febiger, 1950. $6.00.

This atlas on the kidney, consisting of one hundred plates, is divided into two sections, a short one on the normal and a long one on the diseased kidney. The section on pathology is again divided into acute renal failure and chronic renal failure and allied conditions. The author has used the new technical methods, especially the period acid, in preparing his microscopical sections. The plates are accompanied by descriptive text, in which clinical aspects are also discussed. The plate work, type and printing are excellent. The atlas should be in all medical libraries and in all collections on pathology.

NOTICES

ANNOUNCEMENTS

Dr. Harold M. Constantian announces the removal of his office for the practice of urology to the Professional Building, 27 Elm Street, Worcester.

Dr. W. Philip Giddings announces his removal from Boston to Bennington, Vermont, where he is now engaged in the practice of general surgery.

Dr. Sumner H. Hoffman announces the opening of offices for the practice of pediatrics at 1689 Beacon Street, Brookline, and 193 Garden Street, Needham.

Dr. Martin M. Nothman announces the removal of his office for the practice of internal medicine to 311 Commonwealth Avenue, Boston.

Dr. Kenneth J. Welch announces the opening of his office for the practice of general and pediatric surgery at 1101 Beacon Street, Brookline.

CHILDREN'S MEDICAL CENTER

The clinicopathological conferences of the Children's Medical Center will be resumed on Wednesday, September 27, at 12 noon. These conferences will again be held in the amphitheater of the Peter Bent Brigham Hospital.

THE SPRINGFIELD HOSPITAL

The following is the educational program of the Springfield Hospital for the month of October:

Wednesday, October 4. 12 m. Radiology Conference in the Staff Conference Room on the subject "X-Ray Studies of the Abdomen." Dr. John W. Turner.

Saturday, October 7, 12 m. Combined Medicosurgical Grand Rounds in the Staff Conference Room.

Wednesday, October 11. 12 m. Pediatric Conference with Case Presentation in the Staff Conference Room. Dr. Norman A. Pokorny.

Thursday, October 12. 12:15 p.m. Staff Meeting in the Staff Room.

Saturday, October 14. 12 m. Clinicopathological Conference in the Staff Conference Room.

Wednesday, October 18. 12 m. Urology Conference with Case Presentation in the Staff Conference Room. Dr. Lawrence H. Doolittle.

Saturday, October 21. 12 m. Medical Death Review Meeting in the Staff Conference Room.

Tuesday, October 24. 8:30 p.m. Guest Speaker Conference on the subject "The Rh Factor and Its Relation to Intragroup Transfusion Reactions and Hemolytic Disease of the New-Born" in the Staff Conference Room. Dr. Arthur W. Wright, professor of pathology and bacteriology, Albany Medical College, and pathologist-in-chief, Albany Hospital, Albany, New York.

Wednesday, October 25. 12 m. Gynecology Conference with Case Presentation in the Staff Conference Room. Dr. Arthur F. G. Edgelow.

Saturday, October 28. 12 m. Surgical Death Review Meeting in the Staff Conference Room.

NATIONAL GASTROENTEROLOGICAL ASSOCIATION

The fifteenth annual convention of the National Gastroenterological Association will be held at the Hotel Statler in New York City, October 9-11.

Among the outstanding speakers to present papers at the Convention are: Dr. Richard B. Cattell, Lahey Clinic, Boston; Dr. W. Stuart Harrington, Mayo Clinic, Rochester, Minnesota; Dr. W. J. Merle Scott, Rochester, New York; Dr. John B. O'Donoghue, Chicago, Illinois; Dr. Maurice Feldman, Baltimore, Maryland; and Dr. Edward T. Lewison, Baltimore, Maryland.

At the annual banquet, to be held at the Hotel Statler on Tuesday evening, October 10, the winner of the National Gastroenterological Association 1950 Prize Award Contest for the best unpublished contribution on gastroenterology and allied subjects will receive the prize of $100 and a certificate of merit.

Immediately after the convention, the Association is conducting a course in postgraduate gastroenterology at the Hotel Statler in New York City, October 12-14.

Further information concerning the program and details of the course may be obtained from the secretary, National Gastroenterological Association, 1819 Broadway, New York, 23, New York.

EXAMINATION FOR POSITION OF SUPERVISING PSYCHIATRIST IN NEW YORK STATE MENTAL HOSPITALS

Applications may be filed up to September 29 for an open competitive examination for the position of supervising psychiatrist in state mental hospitals to be held on November 4, 1950, by the New York State Department of Civil Service. The examination will be conducted at about 40 centers in New York State and at other locations to accommodate out-of-state applicants.

Although New York State residence and United States citizenship are usually required of applicants for civil-service positions, in this case both requirements have been waived, except for a few jobs in institutions for the criminally insane to which only citizens may be appointed.

Candidates must have completed two years of residency in psychiatry in an approved hospital and two years of experience as a member of the staff of a psychiatric hospital, or a satisfactory equivalent. They must also be eligible to enter the examination for a license to practice medicine in New York State.

Complete details and application blanks may be obtained from the New York State Department of Civil Service, Albany.

REFRESHER COURSE FOR TECHNICIANS IN PROTHROMBIN AND CLOTTING-TIME DETERMINATIONS

A laboratory course in prothrombin and clotting-time determinations for technicians is being given at Newton-Wellesley Hospital on Mondays, Tuesdays and Wednesdays by the Division of Cancer and Other Chronic Diseases in cooperation with the Newton Heart Demonstration Program. The course began in July and will continue through December.

A questionnaire recently mailed to all hospital and clinical laboratories of Massachusetts revealed that there is considerable interest in this type of training for technicians. The course consists of theoretical information and individual instruction in performance of the test. It is given without charge to a qualified technician of any laboratory desiring it. Registrations are still being accepted for the three-day course. Room and board are available at the hospital at minimal charge for those who need accommodation. Applicants are requested to communicate with Dr. H. L. Lombard, Division of Cancer and Other Chronic Diseases, 100 Nashua Street, Boston, as soon as possible.

SOCIETY MEETINGS AND CONFERENCES

SEPTEMBER 26–29. American Roentgen Ray Society. Page 240, issue of August 10.

SEPTEMBER 27. American Medical Writers' Association. Page xi, issue of July 13.

SEPTEMBER 27–29. Mississippi Valley Medical Society. Page 991, issue of December 15.

OCTOBER 3. Massachusetts Academy of General Practice. Boston City Hospital and Hotel Kenmore.

OCTOBER 3. Conference on Alcoholism. Page 430, issue of September 14.

OCTOBER 3 AND 4. Massachusetts Chapter, American Academy of General Practice. Page 430, issue of September 14.

OCTOBER 4–24. The Springfield Hospital. Notice above.

OCTOBER 6–MAY 11. Massachusetts Department of Mental Health. Postgraduate Seminar in Neurology and Psychiatry. Page 324, issue of August 24.

OCTOBER 9–11. National Gastroenterological Association. Notice above.

OCTOBER 9–20. New York Academy of Medicine. Page 430, issue of September 14.

OCTOBER 10. Massachusetts Society of Anesthesiologists. Page 430, issue of September 14.

OCTOBER 12–14. American Association of Blood Banks. Page 428, issue of March 16.

OCTOBER 13. Chemotherapy — New Preparations, Their Efficacy and Effects. Dr. Chester S. Keefer. Pentucket Association of Physicians. 8:30 p.m. Haverhill.

(Notices concluded on page xv)

NOTICES (*Concluded from page 470*)

OCTOBER 14–19. American Academy of Pediatrics. Page 962, issue of June 15.

OCTOBER 23–27. American College of Surgeons. Page xi, issue of June 29.

OCTOBER 23–28. Medicomilitary Symposium for Officers of Fourth Naval District. Page 34, issue of July 6.

OCTOBER 28. Massachusetts Association of Medical Technologists. Page 324, issue of August 24.

OCTOBER 30–NOVEMBER 3. American Public Health Association. Page 240, issue of August 10.

OCTOBER 31–NOVEMBER 3. International College of Surgeons. Page 170, issue of July 27.

NOVEMBER 1. New England Obstetrical and Gynecological Society. Hotel Somerset, Boston.

NOVEMBER 1. Hampshire District Medical Society. Page 170, issue of July 27.

NOVEMBER 5 AND 6. American Society for the Study of Arteriosclerosis. Page 170, issue of July 27.

NOVEMBER 6–8. New England Postgraduate Assembly. Hotel Statler, Boston.

NOVEMBER 10. American Trudeau Society. Page 280, issue of August 17.

JANUARY 31. American Academy of Orthopaedic Surgery (see Kappa Delta Award for Research in Orthopedic Surgery). Page 736, issue of May 4.

APRIL 9–13. American College of Physicians. Page 962, issue of June 15.

MAY 24–26. American Goiter Association. Columbus, Ohio.

DISTRICT MEDICAL SOCIETY

HAMPSHIRE

NOVEMBER 1. 4:30 p.m. Northampton State Hospital.

JANUARY 3. 4:30 p.m. Veterans Administration Hospital, Northampton.

MARCH 7. 4:30 p.m. Cooley-Dickinson Hospital, Northampton.

MAY 2. 4:30 p.m. Annual Meeting. Jones Library, Amherst.

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING THURSDAY, SEPTEMBER 28

THURSDAY, SEPTEMBER 28

*9:00–10:00 a.m. Grand Rounds. House of the Good Samaritan.

FRIDAY, SEPTEMBER 29

*9:00 a.m.–12:00 m. Combined Medical and Surgical Staff Rounds. Peter Bent Brigham Hospital.

*10:00 a.m. Surgical Clinic. South End Health Unit, 57 East Concord Street, Boston.

*1:30 p.m. Tumor Clinic. Out-Patient Department, Mount Auburn Hospital, Cambridge.

MONDAY, OCTOBER 2

*11:30 a.m.–12:15 p.m. Clinical Conference. South End Health Unit, 57 East Concord Street, Boston. Dr. Cleaveland Floyd in charge.

*12:15–1:15 p.m. Clinicopathological Conference. Main Amphitheater, Peter Bent Brigham Hospital.

TUESDAY, OCTOBER 3

*12:15–1:15 p.m. Clinicoroentgenological Conference. Peter Bent Brigham Hospital.

*1:30–2:30 p.m. Pediatric Rounds. Burnham Memorial Hospital for Children, Massachusetts General Hospital.

WEDNESDAY, OCTOBER 4

*12:00 m. X-Ray Conference. Margaret Jewett Hall, Mount Auburn Hospital, Cambridge.

*12:00 m.–1:00 p.m. Clinicopathological Conference. (Children's Medical Center.) Amphitheater, Peter Bent Brigham Hospital.

*Open to the medical profession.

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For further information apply to the DEAN, BOSTON UNIVERSITY SCHOOL OF MEDICINE, 80 East Concord Street, Boston, Massachusetts.

*There will be no exercise on November 8 because of the New England Postgraduate Assembly.

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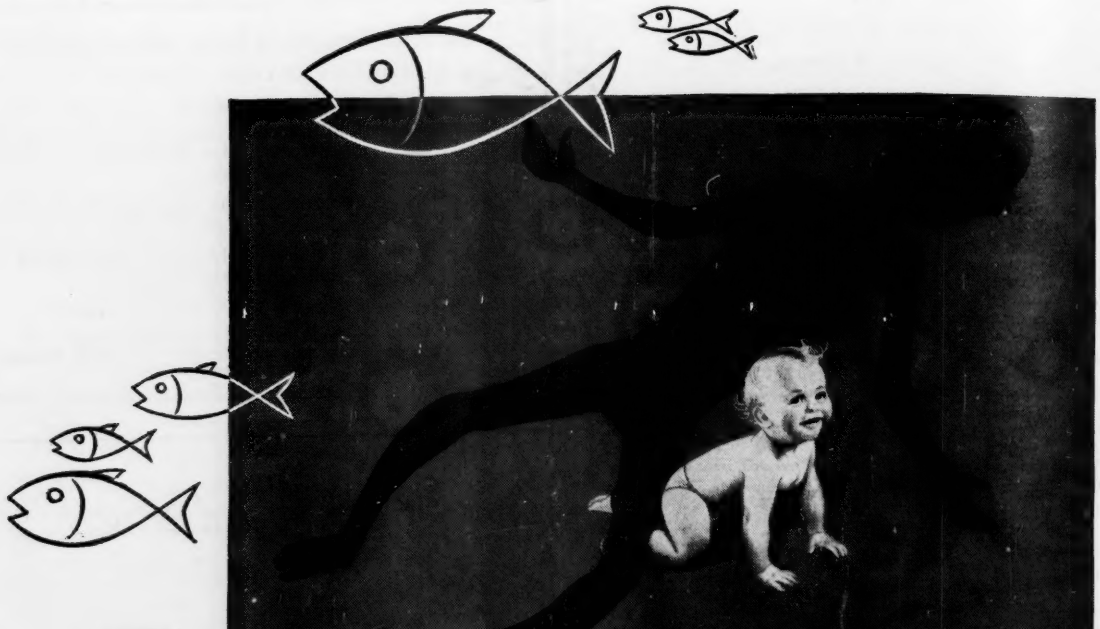

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